The Journal of Thoracic Surgery

VOL. 32 SEPTEMBER, 1956 No. 3

Original Communications

CONGENITAL DIAPHRAGMATIC HERNIA AND HYPOPLASTIC LUNG

A CLINICAL EVALUATION

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CONGENITAL diaphragmatic hernia is reported to be a surgically correctible condition with satisfactory results and a low mortality rate.[1] Published series[2-7] of successful surgical closures of this defect would seem to indicate that operative intervention promptly after birth is mandatory for survival. However, this developmental failure of closure of the pleuroperitoneal sinus, or foramen of Bochdalek, is a relatively rare condition which frequently is not diagnosed until an infant reaches the autopsy table. The serious respiratory embarrassment, thought to be the result of abdominal viscera in the chest, often causes death in the first few minutes of life. In those patients coming to surgery, and particularly in the newborn infant, this disturbed physiology is a significant hazard.

It has been our observation that the compressed and hypoplastic lung in the previously occupied pleural space could not be expanded after removing the abdominal organs. Mention of this problem is notably lacking in the surgical reviews, although association of the two conditions was reported as early as 1893 by Schmit.[8] Dorsey,[9] Tolins,[10] and Ladd and Gross[4] did mention atelectatic lung and respiratory difficulties after operation, but failed to recognize hypoplasia.

The reported clinical experience with congenital diaphragmatic hernia reveals a wide variation in operative results from Truesdale's[3] survival rate of 92 per cent to the 43 per cent survival of the 7 cases reported by Baumgartner and Scott.[11] Contrary to common belief, the over-all survival in this

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Read at the Thirty-sixth Annual Meeting of The American Association for Thoracic Surgery at Miami Beach, Fla., May 7 to 9, 1956.

anomaly is far from satisfactory,[12, 13] and the observations of pathologists are distinctly less encouraging. Edith Potter,[14] in discussing congenital diaphragmatic hernia in her text on infant pathology, states, "In our experience associated pulmonary hypoplasia has been so great that the lungs were incapable of supporting extra-uterine existence." More recently, Campanale and Rowland[15] have reported on this neglected aspect of the problem. To our knowledge, however, there have been no observations on the incidence of hypoplastic lung in congenital hernias of the diaphragm, either in the surgically correctible group[1-7] or in those studied at post mortem.[16] This discrepancy between the optimism of the surgical reports and the less favorable observations of the pathologist suggested the value of further investigation to determine the factors influencing survival.

TABLE I

CONGENITAL DIAPHRAGMATIC HERNIA

47 CASES — 29 DEATHS

38% SURVIVAL

NEONATAL PATIENTS		OLDER PATIENTS (14 DAYS+)	
31 CASES — 27 DEATHS		16 CASES — 2 DEATHS	
13% SURVIVAL		88% SURVIVAL	
NO SURGERY	OPERATED	NO SURGERY	OPERATED
19 CASES — 19 DEATHS	12 CASES — 8 DEATHS	4 CASES — 1 DEATH	12 CASES — 1 DEATH
0% SURVIVAL	33% SURVIVAL *	75% SURVIVAL	92% SURVIVAL

SURGICAL MORTALITY 38%

* OPERATED AT 7 DAYS, 5 DAYS, 2 DAYS & 1 DAY

Hospital records and autopsy protocols were reviewed for all cases of congenital diaphragmatic hernia in eleven San Francisco hospitals for as long as records were catalogued, up to twenty years. Hernias through the foramen of Morgagni, esophageal hiatal hernias, eventration of the diaphragm, and all adult hernias were excluded from the series. A total of 47 cases were analyzed for pregnancy factors, obstetrical course, birth weight, presenting signs, time of operation, operative findings, length of survival, and autopsy observations. These data yielded no pertinent information of value in determining the cause or prognosis of the disease. No pregnancies were complicated by disease; obstetrical delivery was unremarkable; birth weights were normal except for 3 infants weighing under five pounds. Associated congenital anomalies were rare. Two patients in the series were consecutive siblings of the same parents, fourteen months apart.

The over-all mortality rate was 62 per cent which was comprised largely of the newborn infants that never reached surgery. Conversely, almost all of

the surviving patients had passed the early neonatal period (2 weeks to 2½ years) before coming to surgery. Since these two groups apparently are not comparable, they are analyzed separately to emphasize the prognostic differences and in order to consider the management problems in the newborn group (Table I). The 87 per cent combined mortality in the early group is in striking contrast to the 12 per cent fatalities in the older group. Of greater importance is the difference in operative results between the two groups, each with 12 patients operated upon; among the newborn patients there were eight deaths, whereas among the older patients there was only one. Furthermore, 2 of the 4 survivors in the early group were 5 and 7 days old, respectively, at the time of operation. In the older group, 7 patients were between 18 days and 8 weeks old; the others ranged from 6 months to 2½ years. The only fatality was in a 6-month-old child who presented with bronchopneumonia.

Unfortunately, both operative reports and autopsy protocols were often lacking in detailed description of size and expandability of the lung. Table II summarizes these surgical observations concerning lung appearance; in

TABLE II. SURGICAL OBSERVATIONS ON LUNG EXPANSION IN CONGENITAL DIAPHRAGMATIC HERNIA

Satisfactory lung expansion	5
Partial lung expansion	1
Little or no expansion from small nubbin	10
No comment in operative note	8

only 5 of 24 patients was satisfactory lung expansion described, whereas in 10 cases, the surgeon noted that the lung remained small and collapsed. Autopsy observations (Table III) indicate that in size the lung on the hernial

TABLE III. CONGENITAL DIAPHRAGMATIC HERNIA AUTOPSIED LUNG WEIGHT RATIOS

LEFT	RIGHT	RATIO
1.5	11.6	0.13
4.5	27	0.17
6	30	0.20
2	9	0.22
10	46	0.22
2.5	10	0.25
7	25	0.28
9	26	0.35
6.5	17	0.41
4.0	9.5	0.42
8	*3.5*	0.44
11.3	25	0.45
33	55	0.60
10	15	0.66
15	*10*	0.66
10	11	0.91
"One-third"		(0.33)
"One-third"		(0.33)
"Much smaller"		
"Small, poorly developed"	"Normal"	
"Definitely smaller"		
	Average Ratio	0.39

Note: Side of hernia in italics.

side is often only a small fraction of the contralateral lung (average ratio: 0.39). Perhaps of greater significance is the total lung weight (Table IV) which is almost invariably far below the predicted norm according to the figures published by Potter and Adair[17] (Fig. 1). Since the pleuroperitoneal

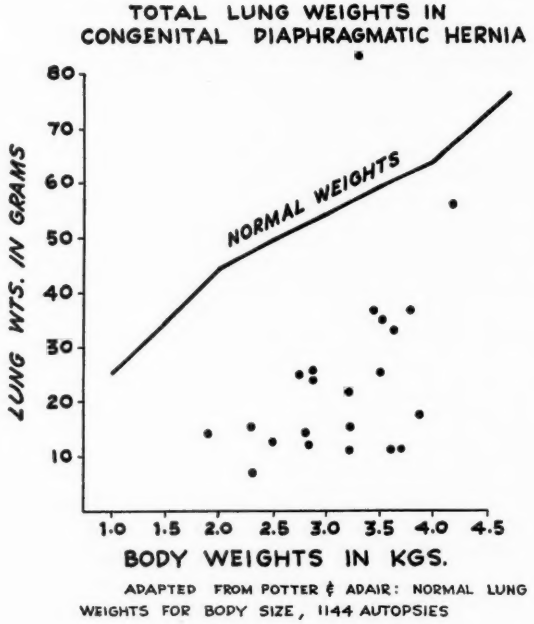


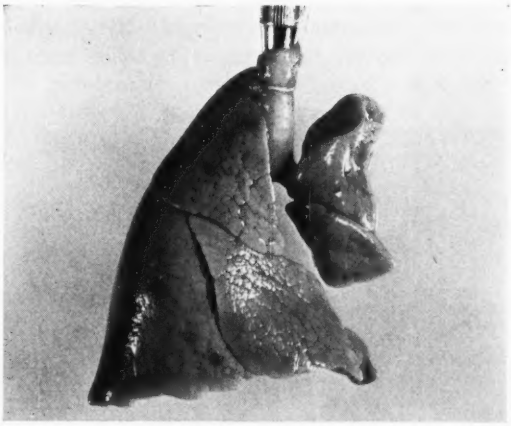
Fig. 1.

TABLE IV. CONGENITAL DIAPHRAGMATIC HERNIA AUTOPSY LUNG WEIGHTS

COMBINED LUNG WT. (GRAMS)	*ESTIMATED NORMAL WT. (GRAMS)	PER CENT OF NORMAL
7	48	15
11	62	18
12	61	19
12	57	21
12	53	23
13	53	24
14	42	32
14	52	27
15	48	31
21	57	37
22	53	41
24	53	45
25	52	48
25	59	43
32	61	52
35	60	59
36	63	57
37	59	62
56	67	84
88	58	138
	Average per cent of normal lung weight	44

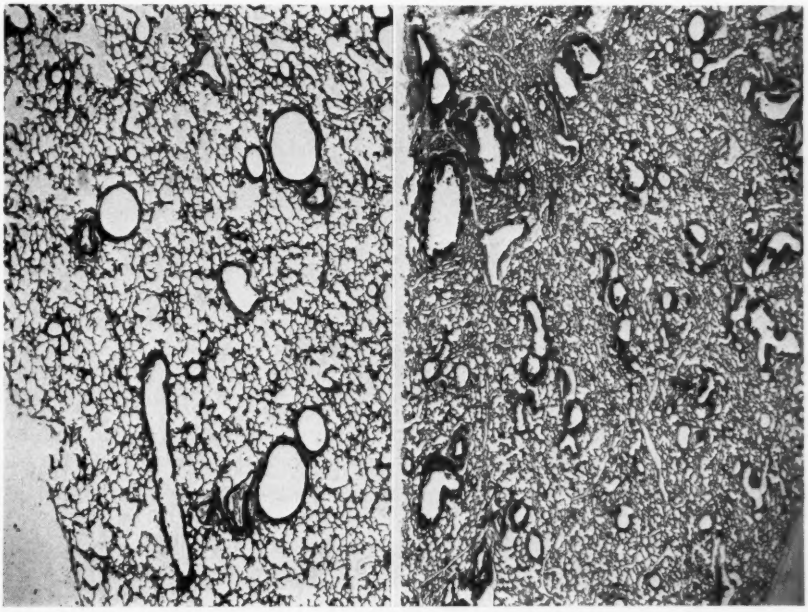
*From Potter and Adair[17]: average infant autopsy lung weight according to body weight.

sinus normally closes in the fourth fetal month, it is not surprising that continued occupation of the pleural space interferes with lung growth on one side, but it is of interest that the combined lung weight should be less than



Right *Left*

Fig. 2.—Inflated lungs of patient with congenital diaphragmatic hernia which caused death a few minutes after birth. Note left lung is very small, even under pressure. Combined lung weight 12 Gm. (body weight, 3,200 Gm.); normal for this infant about 57 Gm.

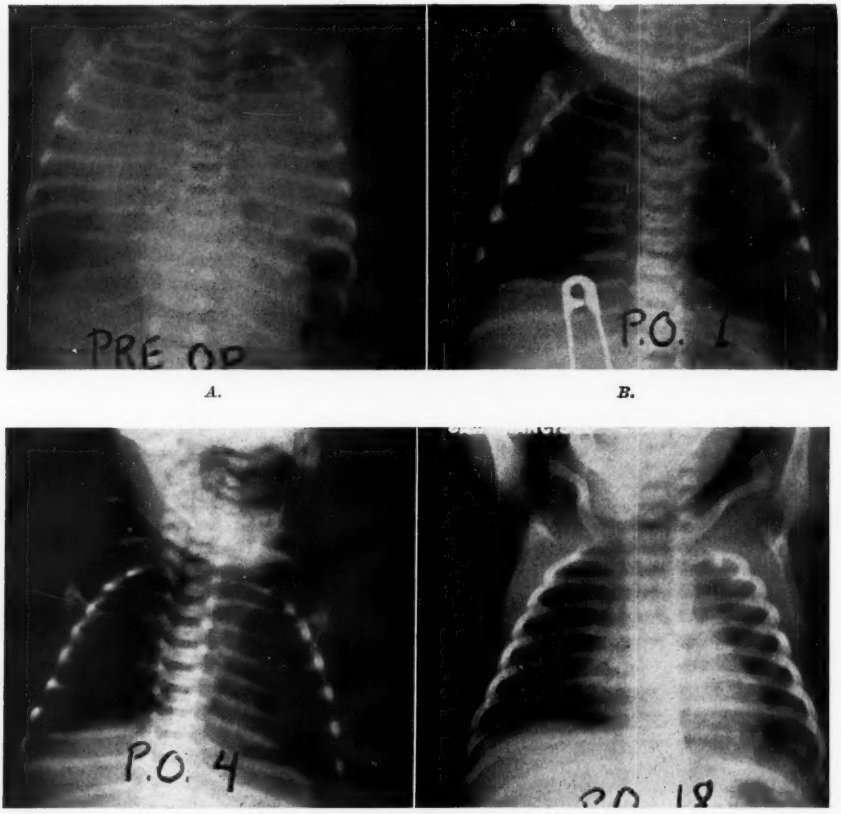


Left *Right*

Fig. 3.—Photomicrographs of inflated autopsied lungs shown in Fig. 2. Note comparable size of vessels and bronchi, small alveolar spaces, thickened alveolar membrane, and absence of atelectasis on left side. (×10; reduced ⅕.)

50 per cent of normal in the majority of autopsied cases (Fig. 2). Microscopic sections of the undeveloped lung showed variably thickened alveolar septa, thick pleura, and some cystic dilatation in sparse alveolar tissue (Fig. 3), but the bronchi and blood vessels were of normal size.

Postoperative roentgenograms demonstrated a variable pattern. In at least 3 cases, the undeveloped lung on the side of the hernia was not immediately expanded but was observed to fill out over a period of several days or



A. *B.*

C. *D.*

Fig. 4.—Serial chest roentgenograms on successfully repaired congenital diaphragmatic hernia in a newborn patient. Note gradual lung expansion on the left. *A*, Preoperative; *B*, first day postoperative; *C*, fourth day postoperative; and *D*, eighteenth day postoperative, fully expanded.

weeks (Fig. 4). Whether these lungs are the emphysematous results of an overexpanded hypoplastic organ, or the true growth of new alveolar tissues, is undetermined. The fact that there was no apparent shift of the flexible mediastinum suggests that the underdeveloped lung must still possess a growth potential. What effect delaying surgery would have on this process is also undetermined.

Statistical analysis of the cause of death was impossible from the material available. In some instances, other anomalies or surgical complications could share the blame, but in general the autopsy observations were less revealing than the clinical course marked by respiratory distress. Tension pneumothorax was a post-mortem finding in 4 operated patients and suggests that vigorous attempts to evacuate the pleural space may lead to rupture of the hypoplastic lung. Smith,[18] however, showed that it took pressures between 20 and 30 cm. of water to expand the normal lung at birth.

DISCUSSION

It is possible that clinical inexperience, technical difficulties, and other hazards of operating on the newborn infant are responsible for the high mortality rate. However, it is significant that the surgical results are distinctly better under the same circumstances after two weeks of life and better respiratory compensation. Other surgical procedures are tolerated by the newborn child without significantly greater mortality than after a few weeks of life. Undoubtedly the process of natural selection in the early neonatal period removes those patients with inadequate respiratory capacity. But, it is likely that this period is also of positive value in improving the gradually acquired ventilatory capacity of an infant and rendering him a better surgical candidate after a few days despite the hernial contents in the chest. Engel[19] has pointed out that even the normal newborn infant has a very poor pulmonary reserve and a very high physiologic dead space; alveolar air filling is not complete for several days,[20] during which time ventilation improves significantly.

Proponents of early surgical intervention would argue that no harm is done in an unsuccessful attempt to correct those whose unpredictable fate has already been sealed. It would be their hope to salvage the borderline patient who might have an expansible lung and survive if the mechanical pressure is removed, but who otherwise would not survive. It is our feeling, however, that more patients with marginal respiratory capacity at birth will survive if surgical intervention is delayed ten days than if operation is carried out immediately. Obviously those with inadequate capacity will die whether or not they are operated upon.

The surgical literature contains little support for this thesis. Donovan[21] notes the greater hazard in younger patients but urges early operation anyhow; Harrington[6] alone recommends delaying operation. Reports of large diaphragmatic hernias in adults[22, 23] further demonstrate that the disease does not always require immediate correction.

Obviously the dispute cannot be settled without further knowledge, but our study suggests that pulmonary hypoplasia is such a common and serious associated problem that the benefits of early expansion may be overestimated. When surgery is performed, it is essential that every adjunct be used to support the marginal respiration postoperatively. A high oxygen atmosphere alone may not suffice; intermittent gentle positive pressure to aid in alveolar aeration should improve respiratory capacity. Tracheostomy to reduce dead space may be helpful despite its management difficulties in the infant. Drainage of the pleural space is strongly recommended for protection against

tension pneumothorax and to promote gentle and gradual expansion of the hypoplastic lung. Vigorous efforts to expand the lung at operation may cause serious damage and should not be attempted.

SUMMARY

1. Forty-seven cases of congenital diaphragmatic hernia were analyzed for factors determining prognosis.

2. Mortality in the newborn group was 87 per cent as compared to 12 per cent in the older patients (over 14 days of age), suggesting that natural selection plays an important role in the results.

3. Surgical mortality was 67 per cent in the newborn infant and 8 per cent in the older group.

4. Hypoplastic lung was an associated finding in nearly all cases autopsied. Average combined lung weight was 44 per cent of normal.

5. Undeveloped lung on the hernial side was recorded in 10 surgical cases and in 17 autopsied cases with weight ratios from 0.13 to 0.91.

6. On the basis of these data, a thesis is presented for postponing early operation in favor of gradual improvement in marginal ventilatory function.

7. Recommendations are made for improving the management of the patient with inadequate lung tissue.

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Discussion

DR. GABRIEL SELEY, New York, N. Y.—I enjoyed this paper and I would like to report an unusual pulmonary complication and presenting symptoms of a Bochdalek pleural peritoneal hernia. The patient was a 35-year-old housewife whose chief and only complaint was recurring hemoptysis. Roentgenographic studies showed an ill-defined density in the left lower chest. Breath sounds were absent over this area and bronchoscopy showed no disease in the bronchial tree. Because of some translucency present in this area, a hernia was suspected and barium enema showed a large amount of large and small bowel in the left pleural cavity. This patient was operated upon, and upon entering the pleural cavity almost the entire large and small bowel including the cecum and appendix were found. There was no pleural sac. The hernia ring was of fairly good size. In order to reduce the contents, the patient was placed in a practically standing position on the operating table. The contents were reduced and the ring was closed, and an attempt was made to expand the lung. It was noted at this time that the left lower lobe was definitely hypoplastic and that the entire diaphragmatic surface showed a severe constricting ring which coincided with the size of the hernia ring. This portion of the lung could not be re-expanded and was severely congested. The chest was closed in the usual manner with drainage, the patient did well postoperatively and has remained well for five years. There has been no evidence of recurrent hemoptysis.

It is my impression that this patient represents an adult who had a hypoplastic lung with a pleuroperitoneal hernia who obviously survived this complication, and then apparently had an incarceration of the lung in the hernial ring which produced hemoptysis. I would like to ask the essayist whether he has encountered any such case, or if any other members of the Association have seen this complication.

DR. WILLIS J. POTTS, Chicago, Ill.—This is a very fine paper, beautifully presented by Dr. Roe, and I believe just four words of it—"The lung will grow." We are far less concerned about the hypoplastic lung than we are about getting the diaphragm repaired quickly. The ill infants with a diaphragmatic hernia are real emergencies and if not operated upon promptly will die. If the child can live ten to twelve days after birth the hernia usually is not severe, that is, the respiratory space is not too extensively encroached upon by the misplaced intestine. From our experience with infants with diaphragmatic hernia, I would say that the real emergencies are practically always those who do not have a sac. If there is a sac, the extent of herniation of the bowel into the chest is limited and an emergency rarely exists.

Our mortality rate in the newborn infant group of diaphragmatic hernias is 25 per cent. In the older age group, there has been no mortality. Two of the deaths were definitely our fault. The first, in keeping with what Dr. Roe has said, was an infant with a tiny hypoplastic lung as big as the end of my thumb. (Incidentally, the left lung is always small and undeveloped in the infant who is born with a diaphragmatic hernia and has all the abdominal organs in the left chest.) The anesthetist made pressure on the anesthetic bag and blew out the good lung on the right side. Death occurred. It is impossible to dilate the miniature lung. Leave it alone and it will grow and expand in time. The second death illustrates an important point in the immediate postoperative treatment which is now routine. As the last stitch is put in to close the diaphragm, we make negative suction on a catheter in the chest to withdraw as much air as possible from the left chest cavity. The difficulty is that some air may leak into the chest while the abdomen is being closed and thereby prevent complete expansion of the left lung. That is what happened in this case and the child died of anoxia. We now make it routine,

after the abdomen is closed, to aspirate the left chest with a needle and remove as much air as possible with a moderate degree of negative suction. We often can remove as much as 50 c.c. of air from the left chest. The procedure, of course, increases the respiratory space by that much.

We do not drain these chests. There is nothing to drain and, besides, the danger of air getting into the chest through or alongside the tube is considerable. Draw out the air and the lung will expand. I agree with Dr. Roe, "The lung will grow."

DR. JOHN S. CHAMBERS, San Diego, Calif.—In connection with Dr. Roe's paper and Dr. Potts's comments, I would like to show slides of chest x-rays of a 2½-week-old infant with pulmonary agenesis and contralateral diaphragmatic hernia.

(Slide) There was a story of five days of respiratory distress preceding this film. The infant showed a left anterior diaphragmatic hernia through the Morgagni foramen which appeared on both the posteroanterior and lateral films. No aeration at all was seen in the right chest. The heart was pulled toward the right. The question arose as to whether this represented atelectasis, hypoplasia of the lung, or perhaps congenital absence of the lung. Bronchoscopy was performed and only a 0.5 cm. stump of the right main-stem bronchus was found. Following bronchoscopy the diaphragmatic hernia was repaired transabdominally, the pleural cavity not being entered as a hernia sac was present. It was noted at operation that there was marked paradoxical motion with respiration of the abdominal contents through the diaphragmatic hernia. After repair of the hernia, the infant did well.

(Slide) This chest x-ray was taken two years later. The absence of aeration of the right lung is still evident, there being either an atresia or a marked hypoplasia of the lung on the right.

DR. MARK M. RAVITCH, Baltimore, Md.—We should at least make mention of the fact that these children all have, or will have within a few hours of birth, intestinal obstruction, and that they may succumb to intestinal obstruction or gangrene or perforation of the intestine or stomach or, on the right side, strangulation of the liver, regardless of the state of the lung; an additional reason for immediate operation. We take the attitude that operation should be undertaken the moment the diagnosis is made. Unless I misread the slides Dr. Roe presented, he indicated that in those children who were not operated upon immediately after birth, the mortality was almost 100 per cent; and in those who were operated on immediately the mortality was about 33 per cent. We do like the intercostal tube even after the abdominal approach, with constant negative pressure gently bringing out the lung, and make no attempt to forcibly inflate the lung. I did not see in the roentgenograms any catheter in the stomach. The two tubes, one in the stomach to empty it completely, placed the moment the diagnosis is made and constant suction applied, and the one in the thorax, we think are almost as important as anything else which may be done.

DR. OTTO BRANTIGAN, Baltimore, Md.—I too enjoyed this excellent presentation by Dr. Roe. I rise to relate a single experience which may be of help. It is true that there will be hypoplastic lungs, bronchial atresia, or even congenital absence of the lung, so that one cannot expect to fill the pleural space by lung expansion. However, there may be failure of expansion caused by a condition similar to fetal atelectasis where the lung seems reasonably normal if it can once be expanded. I encountered one instance in a newborn infant where the anesthetist was unable to expand the lung on the operated side. We hesitated to apply too much pressure to the intratracheal tube for fear of rupturing the opposite lung. However, in this single instance I was able to grasp the main bronchus between two fingers and occlude it. A No. 20 needle was inserted into the bronchus. A 10 c.c. syringe was used to inject air into the bronchus, which caused beginning expansion of the lung. Once expansion was started the anesthetist was able to control it from that

point on. It did not completely fill the pleural space. It seems that this experience might be repeated. It eliminates the fear of too much pressure on the opposite lung and there seems little to be lost and little danger if carried out with caution.

DR. H. BRODIE STEPHENS, San Francisco, Calif.—I too have enjoyed this presentation of Dr. Roe's. I think the people here will get the point of his paper. In a case that I encountered, I tried to get the hypoplastic lung to expand and I thought that was the way to manage this difficulty, and the lung would not come up. In the postoperative management, we undoubtedly put too much negative pressure on the involved pleural side, and reruptured our repair. That is why Dr. Roe went into this subject and I think this presentation is in order.

Certainly if one encounters a hypoplastic lung at the time of repair, and the lung does not come up readily, then the surgeon should seek any method for expansion. You heard what Dr. Potts had to say, if you leave the lung alone it will come up, and I think that is the essential value of this presentation.

DR. DE WITT C. DAUGHTRY, Miami, Fla.—Dr. Roe has focused our attention upon a very important condition. Foramen of Bochdalek hernia is not a common congenital anomaly but the results are so poor generally that I believe it is worthy of very careful appraisal. Our experience has not been good with this condition and I believe it is in part due to the fact that most of these cases I have seen have deteriorated greatly and are in rather poor condition when thoracic surgical consultation was requested.

It has been rather interesting to me to review the records on these patients and to find that many of them were in fair to good condition at birth and remained so for twenty-four to seventy-two hours before any considerable deterioration of the condition occurred. The failure to recognize these lesions before they became serious or death actually occurred, I believe, is due to failure of careful examination and failure to obtain x-rays of the chest on these newborn infants with respiratory difficulty. I know of a number of cases in which a diagnosis was not even suspected until an autopsy was performed.

I certainly believe it will be a step backward to recommend that any delay in treatment be accepted after the diagnosis is made. This is based on the above statement that many of them remain in good condition for quite some hours or two or three days after birth and then suddenly deteriorate before definitive treatment can be instituted. I would certainly like to make a plea for surgical correction at the earliest possible moment. It seems to me that our salvage rate will be a great deal higher by such management. Of course, the good ones are those without a marked amount of interference with pulmonary function, who may survive for some time or even up to several years of age. But that is no argument against a really aggressive approach to the problem.

There does seem to be a hypoplasia or at least a lung that occupies less than normal volume for the first few days or possibly the first few weeks of life. I am not aware of any cases in which there has not been proper expansion or development over a period of a few days or possibly a few weeks after surgery.

I would like to illustrate what I have been trying to say by showing a slide of the chest x-ray and autopsy findings of a patient who seemed to be in good condition at birth, but slowly deteriorated over a period of forty-eight hours and died within one hour after thoracic surgical consultation was requested and while the anesthetist was preparing the patient for surgery. This slide of the x-ray reveals the left thorax to be filled with abdominal content and the heart and mediastinum displaced almost against the right lateral thoracic cage, revealing only a very small rim of aerated lung at the base and at the apex on the right. In other words, there could not be more than 25 per cent aeration of the right lung. This slide (a colored photograph) taken at the autopsy table, reveals a portion of the stomach and the descending colon in the abdomen, with the appendix protruding from the hernial neck into the abdomen. The next slide shows the remainder of the abdominal contents to be located in the left thorax, marked shift of the heart and medias-

tinum and only a very small rim of aerated right lung. The left lung is very small and completely compressed into the mediastinum. When the right lung was aerated artificially, it seemed entirely normal but aeration of the left lung revealed it to be of about 50 per cent normal volume although it seemed normal in other respects.

This to me very vividly illustrates the seriousness of this problem and why we must proceed promptly to correct it.

DR. BENSON B. ROE, San Francisco, Calif. (Closing).—I should like to thank the discussants both for their generous and their controversial remarks. This we anticipated, and it should be pointed out that we would not necessarily recommend postponing surgery but would like to emphasize again that there is some physiologic evidence to show that the lung's ventilatory capacity does improve gradually over the first few days of life. This of course must be weighed against the well-known complications and causes of death that Dr. Potts has pointed out. It would be foolish to have any controversy with one of Dr. Potts's experience in this field, and I think his emphasis on gradual expansion of the lung is certainly the point we would want to stress.

In reply to Dr. Seley's question about cases appearing in adults, I should like to relate an anecdote provided me by Col. Sanford French: he saw a 30-year-old woman who reported to an Army obstetric clinic and claimed that she was nine months pregnant. Her flat abdomen caused her to be sent to the psychiatric clinic but on her insistence a pregnancy test was done. She proved to be pregnant and was shortly delivered of a full-term infant. Her abdominal contents consisted only of her uterus; the remainder of the abdominal organs were in the left chest. These were replaced and the congenital diaphragmatic hernia was repaired after delivery.

Dr. Chambers' case is interesting. We excluded the Morgagni hernias from this series because they are really a separate entity. Dr. Brantigan's suggestion about injecting the bronchus on the hypoplastic lung side I think should be accepted with some caution since both the microscopic sections and the clinical course in these patients have suggested that cystic dilatation and emphysematous destruction of the interalveolar spaces do take place; in one documented case there was actual rupture of the lung on the hypoplastic side from positive intrabronchial pressure. As Dr. Potts said, the lungs will grow, but let them come out slowly.

CRITICALLY CRUSHED CHESTS

A New Method of Treatment With Continuous Mechanical Hyperventilation to Produce Alkalotic Apnea and Internal Pneumatic Stabilization

Edward E. Avery, M.D.* (by invitation), E. Trier Mörch, Ph.D., M.D.** (by invitation), and Donald W. Benson, M.D.*** (by invitation)
Chicago, Ill.

PATIENTS with severely crushed chests, if still alive on arrival in the hospital emergency room, should be salvageable if prompt treatment is instituted using the physiologic principles employed in thoracic surgery. By the use of a specially designed respirator, delivering fixed volume of gases for intermittent positive pressure endotracheal ventilation, we have effected the recovery of a number of patients, of the sort heretofore considered hopelessly mangled.

Accurate figures of mortality of crushing injuries of the chest are not available in the literature as most articles concern discussions of diagnosis, treatment, and case reports. An analysis of thoracic injuries in the armed forces revealed that these injuries were predominantly the penetrating type, with few crushing injuries treated.[1-8] It is difficult to locate such cases in hospital records because very often the crushing injury is only one of many injuries listed on the final diagnosis record, or the death certificate. It is safe to say that mortality from crushing injuries of the chest is extremely high due to the severe physiologic imbalances created by trauma to the chest wall with the drop in ventilation caused by paradoxical motion of the chest, injury to the lungs, gross destruction of the lung tissue, pulmonary edema, and compression by pneumothorax, as well as the complicating factors such as pneumonia and atelectasis. Associated injuries to other organs, particularly to the brain, contribute to the vicious cycle of events leading to death. Chamberlain[9] has pointed out the similarity between the treatment of accidental chest injuries and the defects that are created in an ordinary thoracic operation. The treatment, such as control of hemorrhage, management of the wound, stabilization of the chest wall, drainage of the pleural cavity, and postoperative management of the tracheobronchial tree are essentially the same. However, after a thoracic operation, the patient is usually in the hands of a team trained in the problems of thoracic surgery and constantly aware of the possible rapid changes in cardiopulmonary dynamics. Thoracic injuries most often occur at industrial sites or on highways far from medical centers. Mortality depends

Read at the Thirty-sixth Annual Meeting of The American Association for Thoracic Surgery at Miami Beach, Fla., May 7 to 9, 1956.

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on the speed with which the local physician can evaluate the trauma and institute emergency and supportive therapy until the specialty teams can be consulted. We can expect an ever increasing number of serious chest injuries because of the steady and inevitable increase in speed and congestion on the highways and airways. Approximately 25 per cent of deaths from traffic accidents are due to chest injuries.[11] It is imperative that all physicians familiarize themselves with emergency management. We have been encouraged by the fact that a number of our patients with severe chest injuries who were rapidly failing with the usual modern means of treatment, quickly stabilized and eventually recovered by the use of continuous mechanical hyperventilation. The first of these cases treated by this method is recorded.[10]

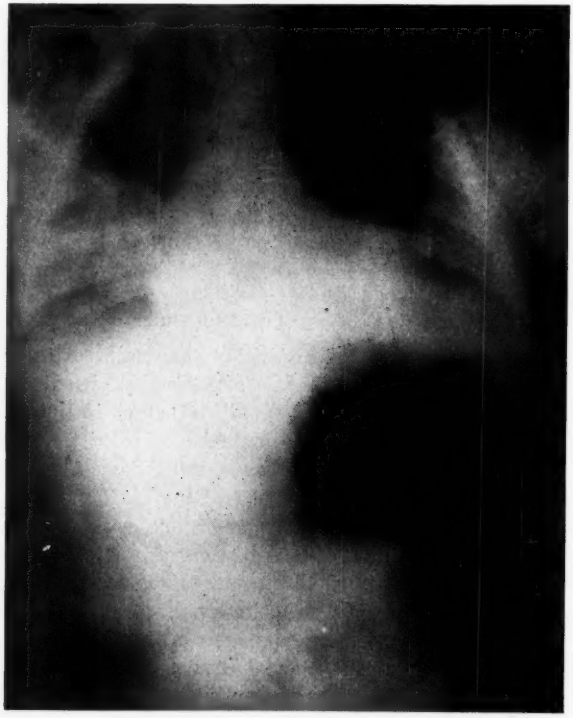

Fig. 1.—X-ray of chest on admission, showing multiple rib fractures, bilateral tension hemopneumothoraces, acute gastric dilatation.

CASE REPORT

In June, 1954, a 51-year-old man was slowly rolled, like pie dough, into an 8-inch space between a diesel locomotive and a steel furnace. He was admitted moribund, in deep shock, with multiple bilateral fractures of all ribs, costochondral separations, bilateral tension hemopneumothoraces, fractures of the sternum, clavicles, pelvis, crushing injuries of the liver and genitourinary tract, paralytic ileus, and acute gastric dilatation (Fig. 1).

The patient was simultaneously treated for shock as bilateral intrapleural catheter water-trap drainage was carried out along with tracheotomy. The anterolateral chest wall was partially stabilized with soft tissue traction by the method of Hudson.[11] Long metal pins were passed under the pectoralis and serratus anterior muscles on each side (Fig. 2). Spreader bows were attached and traction applied to an overhead frame (Fig. 3). Although the paradoxical motion was partially corrected, respiratory acidosis continued due to inadequate ventilation because of actual lung destruction and pulmonary edema (Fig. 4). Various demand flow and pressure cycled respirators were tried. These machines did not ventilate the patient adequately because they were activated by the patient's own weak respiratory efforts or did not deliver constantly adequate exchange of gases. The piston type intermittent positive pressure respirator developed by Mörch[12] was then applied. The patient's condition then improved from a semicomatose state of respiratory acidosis to a more comfortable and alert state of alkalotic apnea. The pH was kept in a range of approximately 7.45. Lung inflation and deflation were mechanically maintained rhythmically and smoothly with loss of all paradoxical motion. This stopped all overriding and grinding motions of the broken rib ends and promoted their healing. Soft tissue traction was discontinued as soon as we realized that complete stabilization of the chest was to be obtained with mechanical ventilation (Fig. 5). When mild respiratory alkalosis was achieved, all respiratory motions ceased. Mechanical hyperventilation was maintained for thirty days until the patient was able to breathe adequately without the assistance of the machine. The CO_2 and pH of the blood were checked twice daily and electrolyte studies carried out as needed. No serious deviations from normal were found in these studies. The patient was discharged from the hospital fifty-one days after the injury and has returned to his work. Since we felt that this treatment by mechanical hyperventilation had allowed the survival of a patient otherwise thought to have a hopeless prognosis, we have now used the same principles of management in a number of severe chest and combined head and chest injuries with equally good results.

General Principles of Treatment.—The principal effect of lung injury and paradoxical motion of the chest wall is to reduce pulmonary ventilation. This, in turn, leads to and aggravates, hypoxia and hypercarbia, pulmonary edema, atelectasis, pneumonitis, and depression of the respiratory center. All of these factors compound one another and lead to death. In the past, the major attention of treatment has been focused on the stabilization of the chest wall to relieve paradoxical motion, and indirectly improve ventilation. Adequate ventilation alone can break the vicious cycle of events and correct all of the noxious contributing factors listed. These efforts to improve ventilation must be rapidly instituted. As in all emergency therapy, it must be remembered that "first things come first." In other words, each situation must be corrected in the order of its urgency.

The patient should have an *upright* chest x-ray immediately on admission to allow accurate evaluation of the injuries. The treatment of shock, the decompression of hemopneumothoraces, and the establishment of a clear airway are usually all of equal urgency because continuation of any one of these alone could cause the rapid demise of the patient. An airway must immediately be established by means of a bronchoscope or an endotracheal tube to aspirate secretions and administer oxygen under positive pressure. A tracheostomy can then be carried out over the tube which can then be withdrawn and replaced in the tracheostomy wound. After these situations are under control, the next problem by order of urgency is that of the paradoxical motion of the chest

Fig. 2.

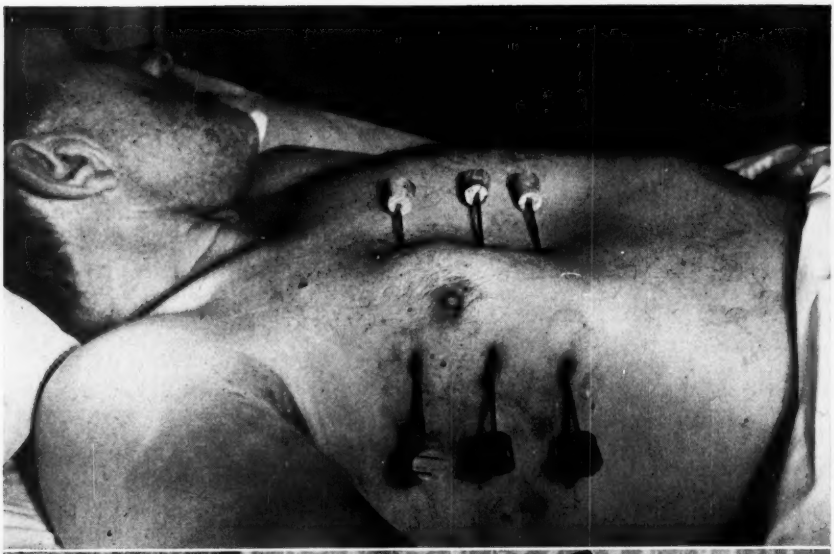

Fig. 3.

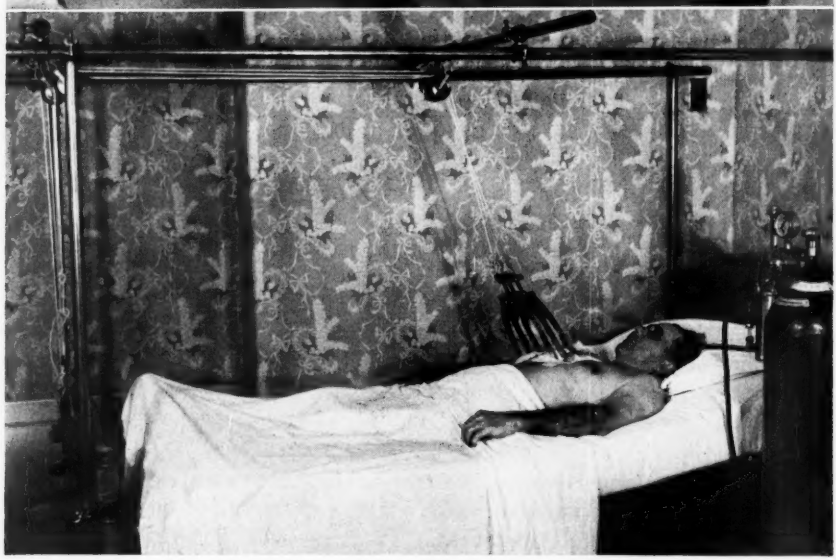

Fig. 2.—Stainless steel pins inserted under pectoralis and serratus anterior fascia for Hudson traction.

Fig. 3.—Hudson traction with spreader bows attached.

Fig. 4.

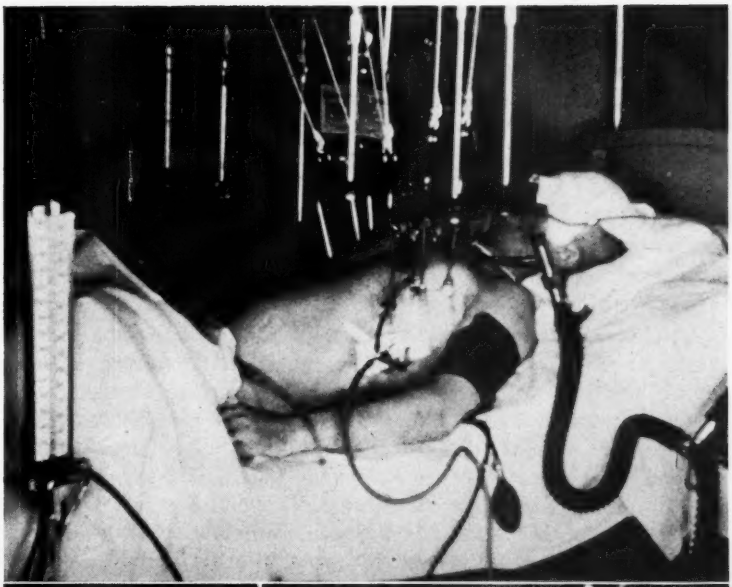

Fig. 5.

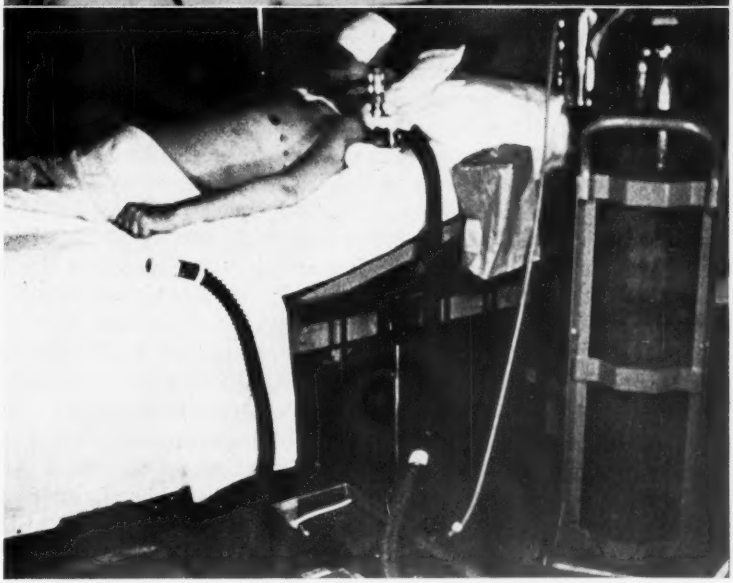

Fig. 4.—The patient reported, with bilaterally applied Hudson traction.

Fig. 5.—Traction removed. Good ventilation with no paradoxical motion of chest on Mörch respirator.

wall. When the bony support of the chest wall is broken, the bellows action of the diaphragm and accessory respiratory muscles, which draw air into the lungs, is markedly reduced. As the diaphragm descends in an attempt to reduce the intrathoracic pressure, the atmospheric pressure compresses the flail chest wall. This reduces, in varying degrees, the amount of air inspired into the lungs; or in effect, enormously increases the amount of dead air space within the lungs. In expiration, as the intrathoracic pressure exceeds the atmospheric pressure, the flail chest bulges outward so that very little air is expired. Thus, a large proportion of the air remains within the confines of the thorax and pendulates back and forth from the alveoli to the tracheobronchial tree with inspiration and expiration. Any diminution of this dead air space will benefit the patient's ventilation.

Carter and Giuseffi[13] have pointed out the advantages accrued from tracheostomy. The dead air space, represented by the volume of the nasal, pharyngeal, and laryngeal air passages which can be short-circuited by tracheostomy, amounts to approximately 100 to 150 c.c. The authors point out that the elimination of this dead space results in more effective ventilation, a diminished resistance to inspired and expired air, and thus reduction of the paradoxical motion of the unstable chest wall. Poor ventilation immediately leads to inadequate absorption of oxygen and elimination of carbon dioxide. The body responds to these stimuli by attempting to increase rate and the depth of respiration. The volume of respiration may be limited by other factors such as partial collapse of the lung due to pneumothorax, hemothorax, actual lung destruction, obstruction of alveoli by pulmonary edema and secretions, painful splinting of the respiratory muscles, and instability of the chest wall due to multiple rib fractures. Increasing the rate of respiration provides little benefit because of the poor volume of exchange. Most of the air motion takes place within the dead air space which has been tremendously increased by the paradoxical motion of the chest wall. To improve ventilation and relieve the hypoxia and hypercarbia that initiate a lethal chain of events, the chest wall must be stabilized. Traction devices may be tried to relieve this paradoxical motion so that the patient can adequately ventilate himself, or adequate ventilation must be provided for the patient by the proper mechanical respirator. Fractures of the ribs and sternum, or costochondral separations, producing only minor degrees of chest wall instability, can be controlled by the usual methods of overhead traction with screws, wires, pins, or tongs.

When the chest wall is badly crushed, particularly bilaterally, adequate stabilization is usually impossible by these traction methods. These patients must be provided with adequate ventilation by mechanical means. The idea of providing intermittent positive pressure oxygen to cases with ventilatory insufficiency is not new. Over 400 years ago, Vesalius of Holland (1542)[14] insufflated gases into the trachea by means of a simple device similar to the fireside bellows. At the turn of the twentieth century, the pioneers of thoracic surgery were using a Fell-O'Dwyer foot bellows apparatus, the positive pressure cabinet of Brauer of Hamburg, and the negative pressure cabinet of

Sauerbruch, the forerunner of the Drinker respirator. More recently, there have been many reports using the modern designed respirators of Engström, Blease, Monaghan, Huxley, Bennett, Emerson, Jefferson, VanBergen, Mörch, and many others[15-21] for ventilatory maintenance of apneic patients, particularly those suffering from bulbospinal poliomyelitis. These machines have also been used on patients suffering from postresection pulmonary insufficiency and acute systemic tetanus.

During World War II, the value of assisted ventilation was realized in crushing injuries of the chest. Positive pressure oxygen was administered by use of a tightly fitting face mask or provided directly through an endotracheal tube connected to an oxygen bag. A Drinker respirator was sometimes used to transport the patients to a treatment center. The value of this type of treatment has not been fully appreciated. Jensen,[22] in his illuminating report, described the pressure relationships of respiration necessary to correct the paradoxical motion of a fractured chest wall. He observed the beneficial results of intermittent oxygen therapy during the emergency phase of treatment and realized that this must be continued until the flail chest had healed. He devised a simple and inexpensive apparatus to deliver positive pressure oxygen through the tracheostomy tube. He found that an adequate gas exchange could often be maintained on a 4 cm. water pressure differential between inspiration and expiration so that the intratracheal pressure never fell below atmospheric pressure on inspiration, and would raise 4 cm. of water above atmospheric pressure on expiration. We have used Jensen's apparatus with good results when the patient had active respiratory movements and there was no associated brain damage.

In many cases, adequate ventilation cannot be maintained with a demand flow apparatus and it is not feasible to increase the expiratory resistance above 4 cm. of water because of the deleterious effects on the circulation. Demand flow respirators are not adequate for many chest injuries because muscle, nerve, and brain damage may block the patient's ability to "demand." Most of the other common respirators now being used are cycled by either time or pressure and operate to deliver a certain pressure. Pressure differentials will vary from individual to individual and often in the same individual from time to time, depending on the variations in the resistances in the pulmonary tree. These resistances are: the flow of gases through the tracheobronchial tree, the frictional resistance between tissues, and the resistance due to the elasticity of the chest wall and lungs often referred to as "pulmonary compliance." To maintain a patient in a steady, and even predetermined, physiologic level, the minute volume must be maintained at a constant, while the pressure differentials are allowed to fluctuate, depending on the elastic properties of the lungs and chest wall and frictional resistance in the tissues and the airway.

Mörch Piston-Type Respirator.—The Mörch respirator was found to be particularly adaptable for the treatment of patients with severe chest injuries (Fig. 6). This machine was first designed and used by E. T. Mörch in 1940, while in Copenhagen.[12] It consists of a piston-type pump driven by an electric

motor and is designed to give a large stroke volume (Fig. 7). The stroke volume is adjustable from 0 to 3,600 c.c. Fresh air, or air-oxygen mixture, is pumped from the cylinder across a humidifier to the tracheostomy. A specially designed "check-valve" is interposed in the system near the tracheostomy tube so that exhalation takes place as soon as the desired stroke volume has been delivered (Fig. 8). The apparatus is ruggedly constructed so that mechanical failures have been nil. A hand-bellows has also been incorporated in the machine so that ventilation can be carried out in case of electrical power failure or when transporting the patient (Fig. 9).

Although it first seemed unreasonable to use an uncuffed tracheostomy tube, the advantages of the uncuffed tube are now obvious.[21] It was first used by one of us (E. T. M.), in 1951.[23]

The Cuffed Tracheostomy Tube.—The use of the cuffed tracheostomy tube (Fig. 10) is disadvantageous in many respects, and it is said to be attended "by all sorts of complications."[24] (1) The soft rubber tracheostomy tube with inflatable tube is much more difficult to insert into the right place in the trachea than the silver tube. The cuffed tube may go into the loose connective tissue outside the trachea; it may not be inserted far enough; or it may be inserted too far so as to enter the right main bronchus so as to obstruct the right upper lobe orifice. (2) The cuff offers resistance on insertion, and may rupture or be dislocated during insertion. (3) The cuff is unreliable and treacherous because it is difficult to keep inflated and the inflated cuff presses against the tracheal mucosa and may cause trauma or even necrosis.

The Uncuffed Tracheostomy Tube.—The uncuffed tracheostomy tube for intermittent positive pressure breathing has been used by us (Fig. 11). It proved satisfactory if a high stroke-volume respirator was used, enabling one to compensate for the leaks. The uncuffed tracheostomy tube is now used routinely for all cases requiring ventilation by tracheostomy. It has been used continuously for periods up to thirteen months in cases of respiratory paralysis due to poliomyelitis. The leak up through the larynx has proved desirable as a safety device against excessive pressures in the lungs and will prevent secretions from entering the trachea by blowing them from the pharynx up toward the mouth where they are easily accessible to the nursing staff.

Care of Tracheostomy.—For tracheostomy, an ordinary Chevalier Jackson silver tracheostomy tube has been modified (E. T. M.) with two swivel joints so that the patient may move his head without impingement of the tube on the trachea.[25] A screw cap allows access for suctioning without actually disconnecting the attached tubing from the respirator.

Proper humidity can usually be maintained by filling the humidifier in the respirator with 5 per cent alcohol-water solution. Additional humidity can be used by inserting a Hi-flow nebulizer in the system. In some cases, distilled water will be sufficient for aerosol. In other cases, bronchial secretions may be viscid, and large plugs or crusts, life-threatening. Diluted Alevaire (1:4)

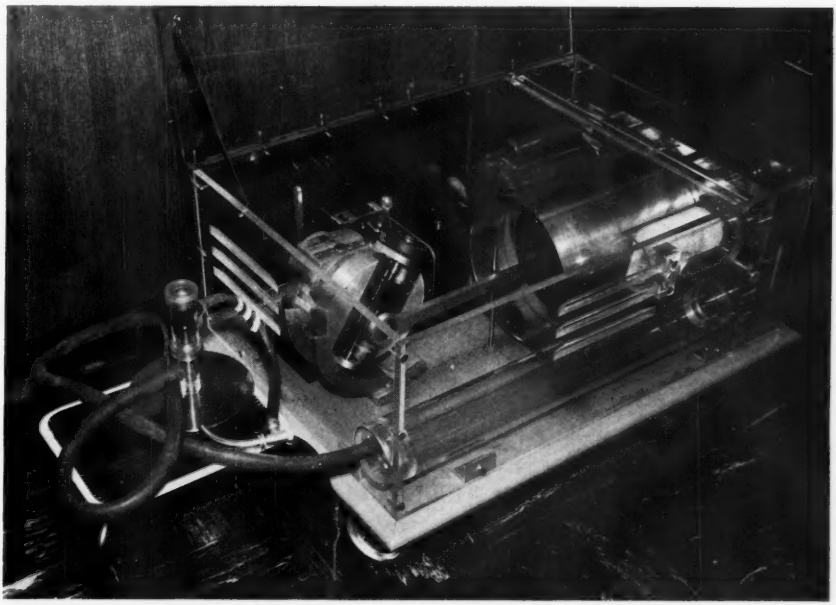

Fig. 6.—Mörch piston respirator connected to plastic check valve and tracheostomy tube.

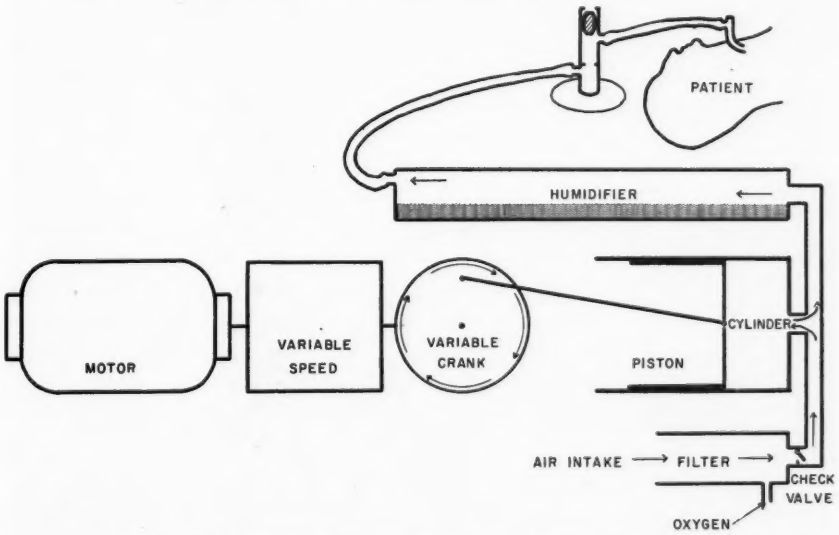

Fig. 7.—Diagram showing the principles of the Mörch piston respirator.

may be used effectively as a detergent and occasionally diluted Tryptar enzyme digestant is necessary. Bronchoscopic aspiration through the tracheostomy can be used as indicated. In chest injuries, tracheobronchial suctioning must be carried out every 15 to 30 minutes because of the large volumes of secretions. To prevent further contamination of the airway, a sterile catheter

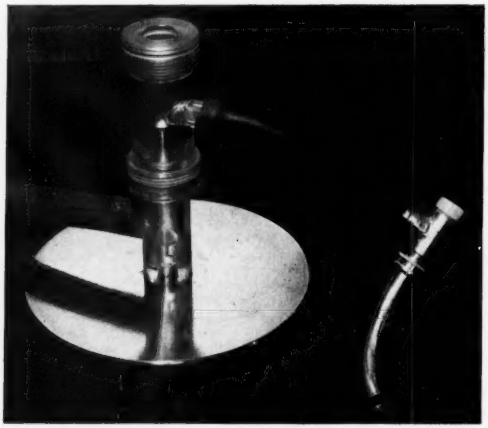

Fig. 8.—Mörch plastic exhalation valve and swiveled, uncuffed, silver tracheostomy tube.

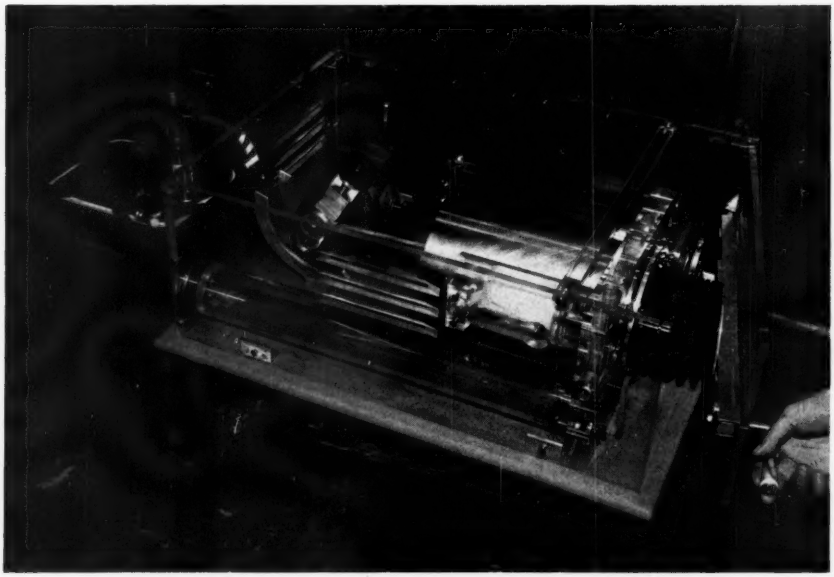

Fig. 9.—Mörch respirator showing emergency hand bellows for use in case of electrical power failure or transportation of patient.

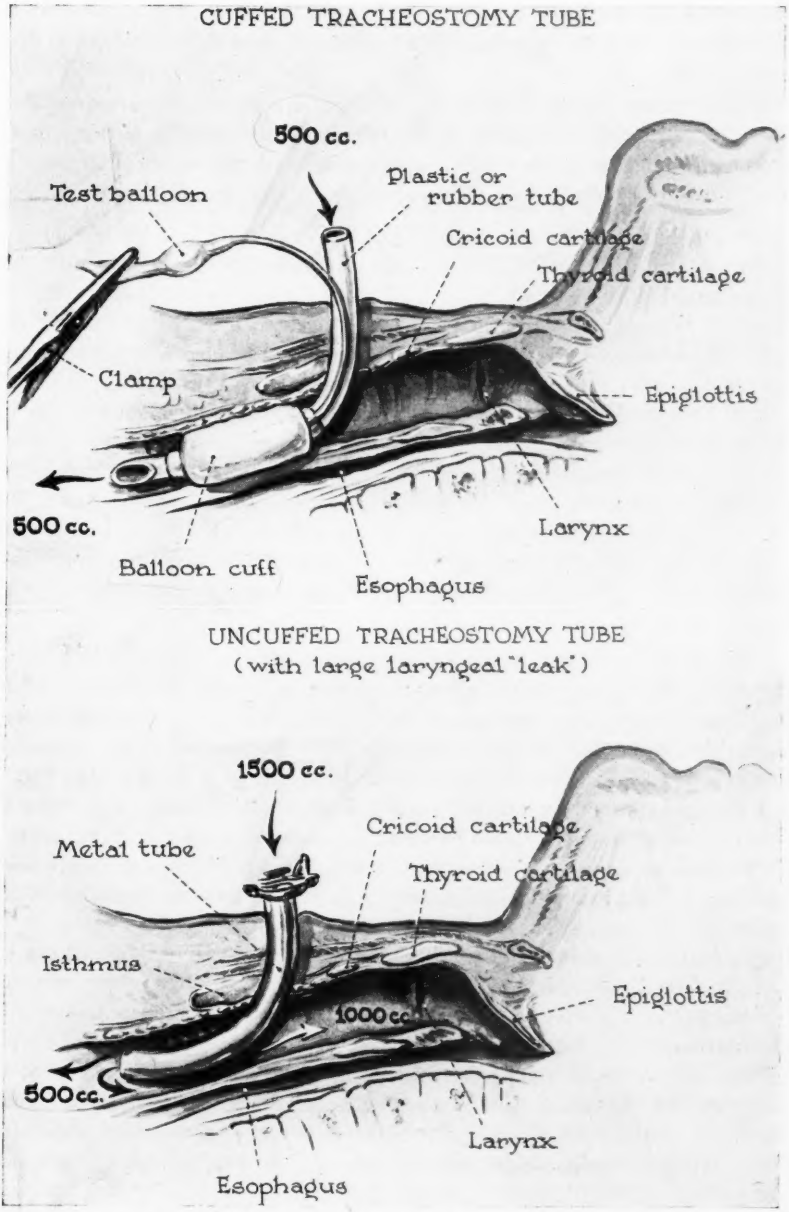

Fig. 10.—Cuffed tracheostomy tube must be airtight for pressure cycled respirators.

Fig. 11.—Uncuffed tracheostomy tube delivers adequate ventilation if respirator stroke volume is sufficient to compensate for laryngeal leak.

should be used with each aspiration. The Coudé curved-tip catheter is the easiest to insert into both the right and left bronchi by merely turning the tip in the correct direction.

Cultures and antibiotic sensitivities are taken on bronchial secretions at appropriate intervals to determine the effective antibiotics to be used parenterally and topically to inhibit tracheobronchial and pulmonary infection.

Proper Respirator Pressure Profile.—Cournand and Motley and their associates[26] found that cardiac output was not decreased with intermittent positive pressure respiration provided that the expiratory phase was slightly longer than the inspiratory phase and when the expiratory pressure was allowed to drop to that of the atmosphere. In other words, normal cardiac output depends more on the type of pressure profile in terms of the length of inspiratory and expiratory phases and the mean intratracheal pressures rather than the peak intratracheal pressure. A proper pressure profile allows for the adequate recovery of circulation during expiration so that blood flow remains constant even over wide ranges of intratracheal pressures. Inspiration is accomplished with a short blast of air occupying only one-third of the respiratory cycle time. The peak inspiratory intratracheal pressures are usually 30 mm. Hg or less. By balancing the stroke volume and rate of respiration against the patient's tracheobronchial resistance and pulmonary compliance a proper pressure profile can be obtained for each patient.

The Maintenance of Adequate Alveolar Ventilation.—There will be adequate oxygenation of the blood when air or gas mixtures have oxygen tensions of 100 mm. Hg or greater. This tension is easily obtained. Therefore, ventilation should be regulated according to the amount of carbon dioxide to be removed.[27] Because of serious alterations that can occur in acid-base and electrolyte balance with abnormal concentrations of carbon dioxide, it is necessary to keep the concentration of this gas within certain limits. It has been found that respiratory acidosis has far more serious consequences than mild respiratory alkalosis; therefore, it is logical to keep the patient in normal balance or even in slight respiratory alkalosis. The Radford nomogram can be used to calculate the minute ventilatory volume on the basis of each patient's metabolic demands.[28] We have found it simpler to keep the body in a state of slight respiratory alkalosis so that we can call upon the brain's respiratory center to help monitor the controls of the mechanical ventilator. By adjusting the stroke volume and rate of the respirator so as to keep the alveolar CO_2 tension just at the level to render the patient apneic we are able to take advantage of this delicate monitoring system. Should the patient benign to make spontaneous respiratory efforts, stroke volume can be slightly increased to render him again apneic. This volume of ventilation should be carefully titrated so as not to hyperventilate the patient massively. Serious deviations in blood chemistry due to hyperventilation can be avoided by checking the pH and CO_2 of the venous blood once or twice daily. If the patient's respiratory center is depressed by asso-

ciated brain damage, more frequent analysis of pH and CO_2 may be necessary. Protein and electrolyte levels should be properly maintained by appropriate studies and therapy.

Rationale of Hyperventilation Therapy.—Although mechanical respirators have had wide application in a variety of pathologic conditions having ventilatory insufficiency, and even in chest injuries, we believe that we are the first to recommend prolonged mechanical *hyperventilation* to produce alkalotic apnea as a therapeutic modality in severe crushing injuries of the chest.[10, 29]

The manner in which hyperventilation counteracts paradoxical respiration and overriding fractured ribs can be explained as a combination of two factors, mechanical and biochemical (Fig. 12).

The mechanical factor is as follows: During *active inspiration,* as the diaphragm descends, the intrathoracic pressure decreases to subatmospheric. The extrathoracic atmospheric pressure, now being greater, pushes the traumatically softened thorax inward and paradoxical motion and overriding of the ribs results. During *active exhalation* the reverse takes place. The intrathoracic pressure is now above the extrathoracic atmospheric pressure and the fractured parts of the bony thorax are pushed outward.

During *passive* (mechanical) *inspiration,* the air is automatically pushed into the lungs under a pressure which exerts a gentle, evenly distributed outward push on all of the softened parts, holding them in their normal position. During *passive exhalation,* the intrathoracic pressure drops toward room pressure so that the inside push gradually diminishes. Because the patient is apneic, no voluntary diaphragmatic action occurs and consequently, no negative intrathoracic pressure develops to produce paradoxical motion. In this way, the alternating positive and subatmospheric pressure during active respiratory efforts has been replaced by a fluctuating positive pressure. The only rib motion is in their normal arcs while they passively ride on this cushion of air as the lungs gently, and passively, expand and contract. All paradoxical motion with overriding and grinding of broken rib ends is stopped by this "internal pneumatic stabilization."

The Biochemical Factor Is as Follows.—During hyperventilation, carbon dioxide is washed out of the lungs. The CO_2 drops in the alveolar air, in the blood, and in the respiratory center, and active respiration ceases. Hypoxia and hypercarbia, having previously aggravated pulmonary and cerebral edema, are now corrected and this trend reversed. The vicious cycle is thus broken by adequate alveolar ventilation. The chest wall now follows the passive variations in pressure produced by the respirator, and paradoxical movements disappear. When a patient with an injured chest is left to breathe by his own voluntary efforts, ventilation will be insufficient and some degree of asphyxia will develop with resultant excitement, restlessness, and confusion. When mechanical ventilation is carried out, hypoxia disappears and with it the central stimulation. If sufficient carbon dioxide is blown out, a mild sedation has been found in most patients. The respiratory muscles can relax because the

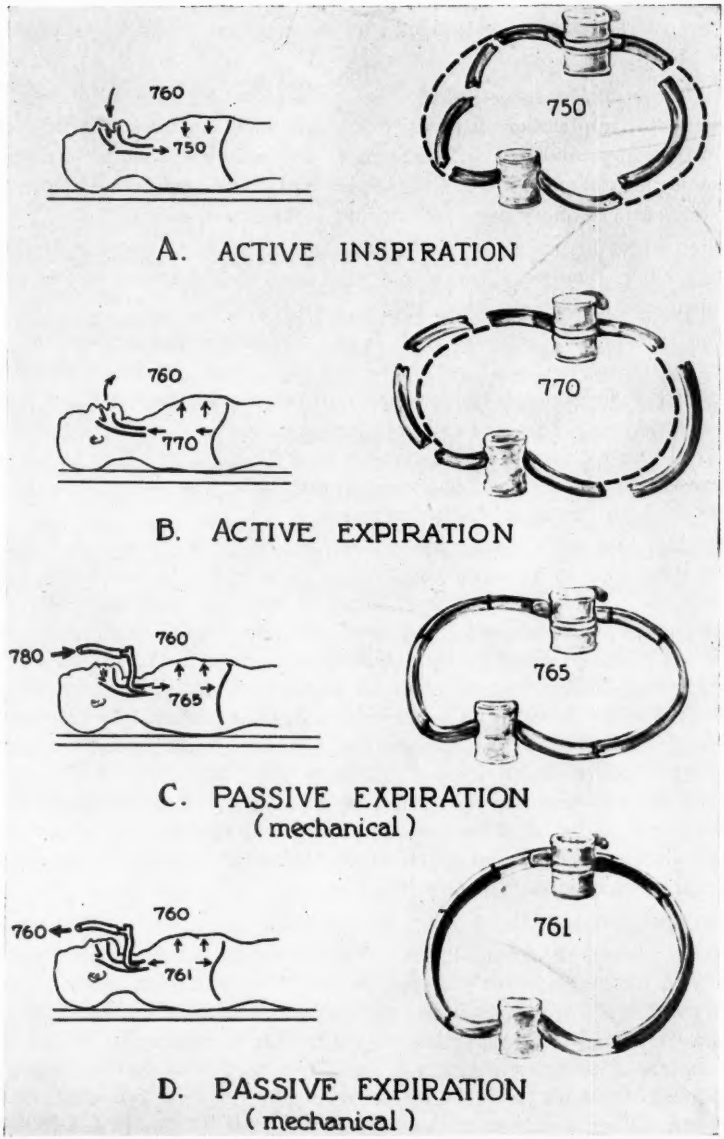

Fig. 12.—*A* and *B* illustrate pressure relationships with active voluntary respiratory efforts causing paradoxical motion of chest wall and overriding and grinding at rib ends.

C and *D* illustrate passive (mechanical) ventilation. Chest wall and ribs ride passively up and down in their own arcs as the lung gently inflates and deflates. All paradoxical motion with overriding and grinding of broken rib ends is stopped by this "internal pneumatic stabilization."

work is done for them and the result is that the patient rests and may even go to sleep. Sedatives may be given as desired for the fear of depression of the respiratory center is now obviated by the mechanical respirator.

A deterrent to the application of prolonged passive mechanical hyperventilation has been the time-honored fear of the adverse effects of the "active hyperventilation syndrome" as seen in hysteria, volunteers, and metabolic acidosis.[30]

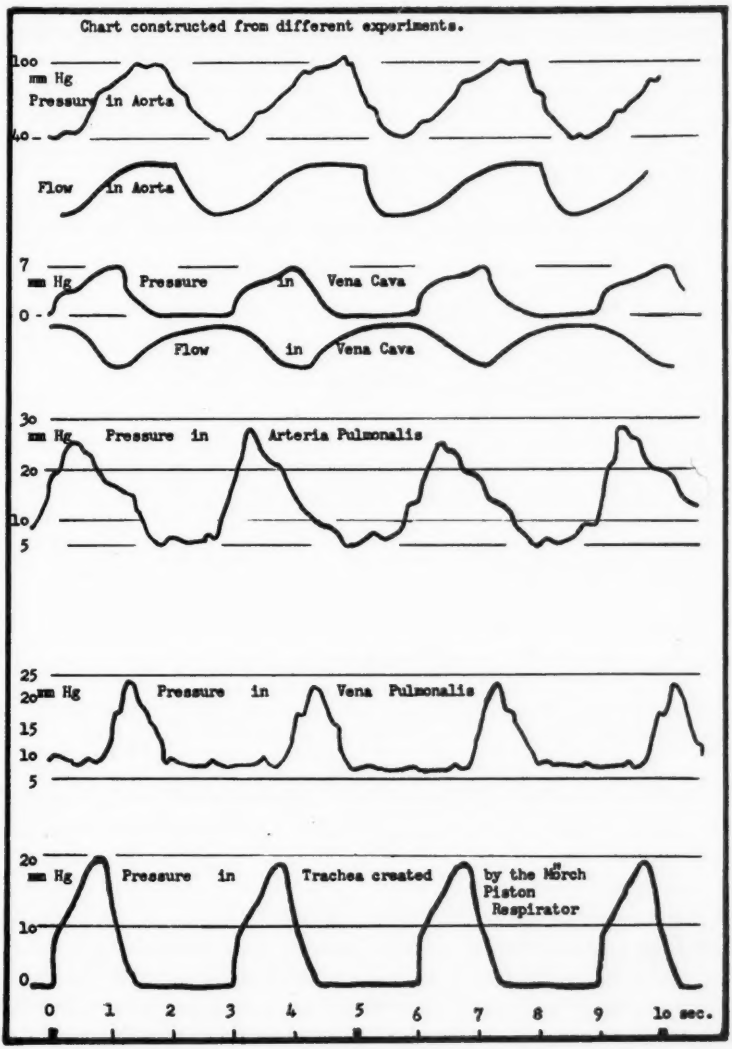

Fig. 13.—This graph shows that pressures and flows in both systemic and pulmonary vessels vary synchronously with the intratracheal pressure. Cardiac output remains practically normal.

These symptoms of tetany, convulsions, unconsciousness, and even death, however, appear to occur only in active hyperventilation. None of these ill effects have been seen in our patients with crushed chests using continuous passive hyperventilation to produce mild respiratory alkalosis for periods of more than a month. Mechanical ventilation has been carried out without adversity in patients for over thirteen months.

Another deterrent to this new method of treating crushed chests has been the numerous references regarding deleterious response to the circulation to intermittent positive pressure insufflation.[31-38] Circulatory changes caused by varying the endotracheal pressures have been studied by us in man and in several experimental animals (dog, rabbit, guinea pig, and bat) (Fig. 13). The circulation has not been significantly disturbed when the pressure within the trachea has the correct amplitude, timing, and mean pressure.

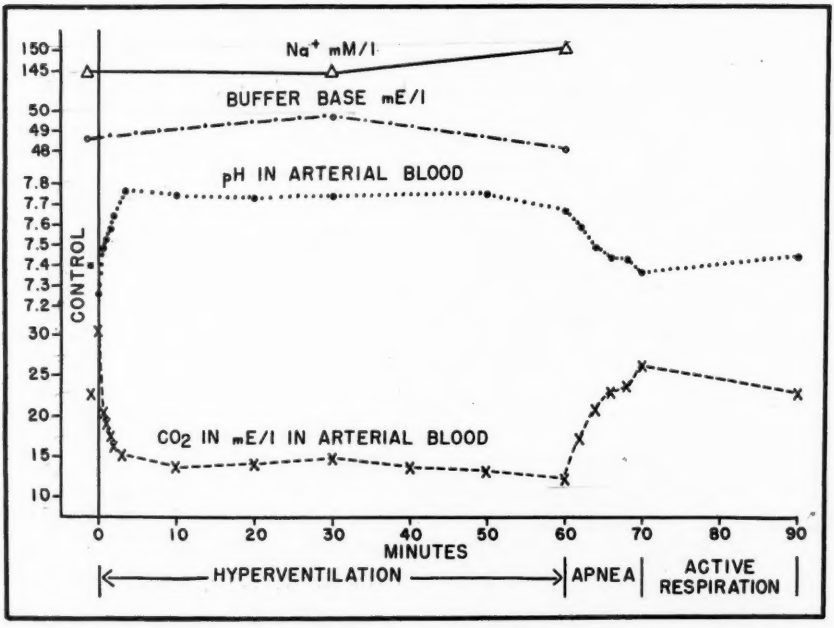

Fig. 14.—Chemical changes in dog experiment with massive hyperventilation.

Changes in blood chemistries have been carefully studied and no undesirable symptoms were found in dogs vigorously ventilated to produce marked respiratory alkalosis (Fig. 14). The chemical changes into and out of respiratory alkalosis took place in a few minutes. Blood chemistries were carefully studied on humans treated on the Mörch respirator by mild respiratory alkalosis and these studies revealed that no serious deviations occurred in pH, CO_2, and electrolyte balance (Fig. 15).

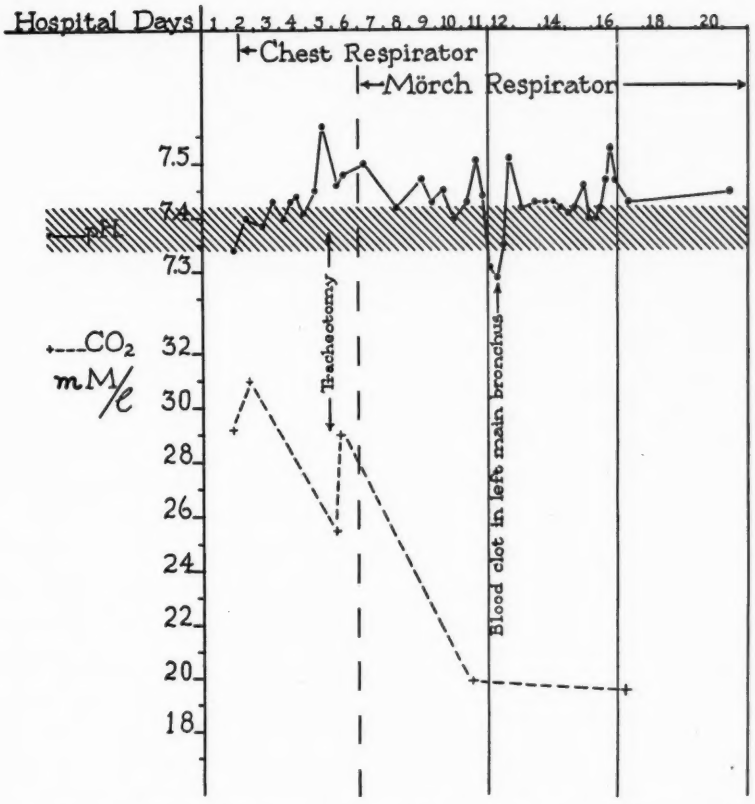

Fig. 15.—Chemical changes in a patient on prolonged mechanical hyperventilation.

SUMMARY AND CONCLUSIONS

1. A new method of treatment of severe crushing injuries of the chest is presented with the use of continuous hyperventilation by means of intermittent positive endotracheal insufflation to produce alkalotic apnea.

2. The most striking benefit of this mechanical hyperventilation treatment is that it is safe and allows the survival of patients with seemingly hopeless prognosis.

3. Other benefits are: correction of paradoxical motion of the chest wall; removal of hypoxia and hypercarbia; absence of pulmonary edema; less sedation is required; no serious deviations in blood chemistry with prolonged mild respiratory alkalosis; no measurable circulatory defects; prompt return of blood chemistries and physiologic responses to normal with cessation of hyperventilation; and no late ill effects.

4. Continuous mechanical ventilation should find a much wider range of application where there is loss of integrity of the chest wall (crushing in-

juries); infections (poliomyelitis, tetanus, etc.); muscle disease (myasthenia gravis, etc.); trauma to the brain (head injuries, postoperative neurosurgical conditions, cerebral vascular accidents); respiratory depression (industrial poisons, suicide, overdosage of medications, and anesthetics); and in ventilatory insufficiency following pulmonary resection. Many of these patients die, not of their primary pathology, but from complications arising from decreased pulmonary ventilation.

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Discussion

DR. HELGE WULFF, Malmö, Sweden.—The excellent equipment so well demonstrated here by Dr. Mörch and his collaborators is no doubt a good contribution to the treatment of risky pulmonary tuberculosis patients operated on with segmental resections and lobectomies, and especially of polio cases. Dr. Trier Mörch has demonstrated the equipment in Scandinavia and, in Sweden, we have used it in a slightly modified type with great success. I have listened to the demonstration with great interest.

DR. B. H. RAMSAY, Los Angeles, Calif.—I wish to congratulate Dr. Avery, Dr. Mörch, and Dr. Benson on their very interesting paper. I think this is something we all need to learn to do and obtain the equipment to do so. In general, treatment of the crushed chest is unsatisfactory, as exemplified by this patient. Two years ago, when 65 years of age, she sustained anterior and posterior fractures of all twelve left ribs. When she survived, everyone concerned was pleased, but the rib fractures, although all healed, had caused displacement and reduction in the left hemithoracic volume by at least 50 per cent. There was little ventilation in the compressed left lung. One year later, a second accident, involving only two of the upper ribs on the right side and a very small pulmonary hematoma, almost resulted in her death as a secondary upper wall atelectasis occurred, due to clotted blood. Only tracheostomy and constant care preserved her. Any nontraumatic right-sided disease such as pneumothorax, or atelectasis, or pneumonia, or even an infarct, would have been similarly serious.

Long ago, surgeons were satisfied if a broken bone healed. Then the disadvantages of nonunion and shortening were appreciated. Accurate reduction and complete return of function are now the expected goal. This must be our idea also in management of the crushed chest. Because of associated injuries, old age and debility, and the need to get people out of bed and back to work, it is not satisfactory to employ routinely balanced traction in a bed frame. During the phase of shock, it is not practicable to wire the fractured ends front and back. I believe that one can reduce the displaced section of the chest by one or more temporary pericostal or peristernal traction sutures, of wire or other material, placed at the center of the flail by direct surgical attack under local anesthesia, attaching these to an external splint similar in all respects to that commonly employed

now in the operation for correcting pectus excavatum. It can be placed laterally or anteriorly. Copper wire, if used, will not easily break or bend, and this can be passed through polyethylene tubing to avoid tissue reaction. I believe emphasis should be placed on retaining the full circumference of the chest and full function thereafter in all instances of chest injury.

DR. N. K. JENSEN, Minneapolis, Minn.—I would like to congratulate Dr. Avery, Dr. Trier Mörch, and Dr. Benson on this excellent contribution. I propose to discuss very briefly the management of chest injuries and particularly to point out that the type and degree of injury are what should condition the method of management.

We believe that the most essential treatment, the most essential maneuver in management of chest injury, particularly a crushing injury of the chest, is a tracheostomy. Many patients with severe chest injuries will do well with a simple tracheostomy. The tracheobronchial secretions can be managed by effective aspiration. The resistance to flow of the respiratory exchange is reduced enough by tracheostomy so that paradoxical motion will subside and the patient will be able to manage his own exchange very well.

The group unable to maintain adequate exchange because of persistence of a flail chest wall after tracheostomy can be managed by simple continuous positive pressure with about 2 cm. of water pressure maintained at all phases of respiration. This maneuver converts ventilation into active expiration while passive inspiration is provided by the positive pressure. In other words, the abdominal muscles take over and exhale against the positive intrapulmonary pressure. The thoracic cage is held steady in an almost full inspiratory position and paradoxical motion stops.

Everything goes well with continuous positive pressure unless one of two situations arises. If tachypnea develops or is present, either because of head injury or respiration too limited in depth because of loss of lung elasticity as in emphysema or for other reasons, then inspiration must be deepened to slow the rate and this requires assistance by mechanical ventilation. Likewise, if abdominal complications develop which result in splinting of the abdominal musculature in association with a flail chest, both mechanisms of respiration are seriously crippled and mechanical ventilation is required.

In summary, I think we should all appreciate the fact that the patient with a severely crushed chest or a fixed thoracic cage who also suffers from a paralyzed or immobilized abdominal musculature must have mechanical ventilation to survive.

DR. JOHN H. GIBBON, Jr., Philadelphia, Pa.—I think we ought to recognize that Avery and Mörch and Benson have given us a very significant and revolutionary contribution toward the surgery of trauma in these difficult cases. All of us, of course, who have been interested in methods of mechanical ventilation have used them during operative procedures and on patients whose respiratory muscles are paralyzed, and have been able to maintain respirations for days by this method. This is the first time, to my knowledge, that I have heard and seen the beautiful results obtained in the stabilization of a flail chest by mechanical ventilation. It seems to me this should have far-reaching consequences in the planning for mass injuries. I hope that members of this Association, and others who are in a position to take care of patients with traumatic injuries of the thorax, will try this method, so that next year a much wider experience can be reported to confirm these very interesting and exciting results.

DR. GEORGE N. J. SOMMER, JR., Trenton, N. J.—I agree that this has been really a splendid paper. I want to mention particularly that this type of injury is to my mind very much on the increase even in my own practice. I came down here yesterday and on the way I passed four automobile accidents of a serious nature. Another point, I chased cars all the way down although I was driving pretty fast. In my opinion, with the speed of travel at the present time, we are going to find more and more drivers of automobiles seriously injured with crushing chest injuries as they crash against steering wheels. Twenty or 25 years ago people were talking about head injuries. The drivers in those cases were usually protected by their feet on the brakes and their grasp on the steering wheel, with

the car going 40 or 50 miles an hour. At the present time, 60 and 70 miles per hour seems to be the usual rate of speed. The drivers are no longer given that protection. I think that is the reason why there is, and is going to be, such a marked increase of these serious injuries. Certainly they are serious and the work done today and shown today shows a method of saving the most seriously injured.

I think Dr. Gibbon made one mistake,* although he does not make very many. But, in the case of mass injuries, these people are going to die. There will never be enough equipment for what he has in mind, or enough personnel to save people if there are thousands and thousands of casualties. The people less severely injured will be saved, but I am afraid that neither he nor I nor anybody else can save these very seriously injured people with a great many injuries.

DR. PETER V. MOULDER, Chicago, Ill.—Dr. Mörch and Dr. Benson have asked me to show you a movie demonstrating the effect of positive pressure on the circulation. The small vessels in the bat wing are filmed through a microscope during periods of varying pressures in the trachea. Air is moved via an intubated tracheostomy. Circulation is first demonstrated during normal respiration, showing a steady flow in the veins and arterioles. With prolonged high, positive pressure there is marked slowing and reversal of flow in the arterioles. With the use of a high pressure of short duration and a negative phase, circulation is nearly normal. Arteriolar flow slows for a short moment at the peak pressure only.

DR. EDWARD E. AVERY, Chicago, Ill. (Closing).—I wish to acknowledge my sincere gratitude to my co-authors, Drs. Mörch and Benson. It has been an unusual pleasure to have the close cooperation of two departments of both Northwestern and Chicago Medical Schools collaborating on this important clinical problem. The Mörch respirator used on these patients represents the culmination of many years of his research in this field. Dr. Mörch's imagination is boundless. Who else would think of intubating a bat! It does point out that this principle of mechanical ventilation can be applied to a 70,000-gram human being or a 5-gram bat.

With regard to Dr. Roe's paper on premature infants with hypoplastic lungs, we are adapting the Mörch respirator for use in these cases. We feel as Dr. Potts does, that these babies must be kept alive long enough to let their underdeveloped lungs grow. We believe that we may be able to provide adequate air exchange to support life by hyperventilating whatever little normal lung tissue is present.

I want to thank all the discussants for their contributions. It is our hope that this mechanical hyperventilation therapy will find wide application for patients with serious chest injuries.

*Dr. Gibbon later told the discussant that he was speaking of civilian disasters with perhaps 100 or 200 injured persons rather than of an atomic attack with thousands of injured.

TRAUMATIC RUPTURE OF THE LEFT-MAIN BRONCHUS SUCCESSFULLY REPAIRED ELEVEN YEARS AFTER INJURY

DANIEL E. MAHAFFEY, M.D. (BY INVITATION), OSCAR CREECH, JR., M.D., HOLLIS G. BOREN, M.D. (BY INVITATION), AND MICHAEL E. DEBAKEY, M.D.
HOUSTON, TEXAS

RUPTURE of one of the major bronchi is now regarded as a relatively common complication of severe trauma to the thorax. Although the condition was diagnosed at necropsy more than fifty years ago,[1, 22, 30, 44] it was not recognized that this injury was compatible with survival until the report of Krinitzke in 1928.[26] Subsequently, Jones and Vinson[21] made the diagnosis clinically, the site of injury being visualized at bronchoscopy. In reporting his experiences with injuries of the chest during World War II, Sanger,[41] in 1945, described 2 cases of traumatic wounds of major bronchi in which he was able to achieve a successful closure. It was not until 1948, however, that Griffith[15] reported the first case to be treated successfully by excision of the strictured segment of bronchus and restoration of bronchial continuity. Operation was performed about eight months after injury and was preceded by several unsuccessful attempts to dilate the stricture. Bronchial anastomosis was performed with No. 38 stainless steel wire, reinforced with fascia. Bronchogram following operation was reported as normal and the vital capacity increased from 2,100 c.c. before operation to 2,700 c.c. eight months after operation.

Since that time many reports have appeared of successful surgical correction of this type of lesion, two hours to fifteen years following injury.[10-12, 16, 32, 35, 37, 38, 40, 42, 43, 45] The most notable case is that recorded by Samson and Evans[40] in which complete rupture of the right main bronchus was successfully corrected, fifteen years after injury.

In spite of the large number of instances of operative treatment of this condition, there is a paucity of data regarding changes in lung function resulting from the injury and from its correction.[15, 40, 48] Recently we have successfully treated a case of traumatic rupture of the left main bronchus eleven years after injury. Pulmonary function studies were made before and on two occasions after operation. Because of its unusual clinical features and the interesting data it affords regarding pulmonary function, this case is reported.

CASE REPORT

W. E., a 32-year-old Negro man, was admitted to the surgical service of the Houston Veterans Administration Hospital, Aug. 31, 1955, with the complaint of exertional dyspnea of eleven years' duration. Dyspnea had appeared following an injury on Dec. 26, 1943,

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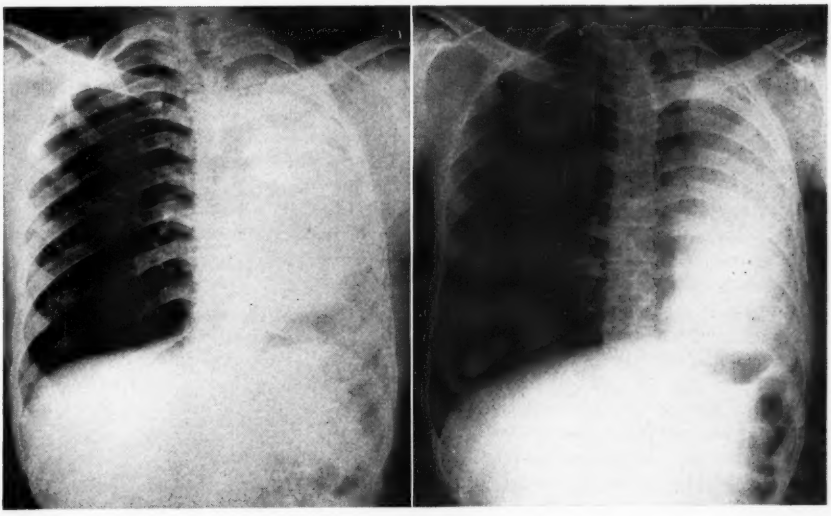
Read at the Thirty-sixth Annual Meeting of The American Association for Thoracic Surgery at Miami Beach, Fla., May 7 to 9, 1956.



A. *B.*

Fig. 1.—*A*, Roentgenogram of the chest two months after injury showing a homogeneous density of the left hemithorax, overdistention of the right lung and displacement of mediastinal structures to the left. *B*, Roentgenogram of the chest approximately eleven years later reveals an increase in volume of the right lung and further movement of the mediastinum to the left.

Fig. 2.—Bronchogram made prior to operation showing the left main bronchus ending blindly. The bronchial pattern of the overdistended right lung is relatively normal.

while in the Navy. The patient fell from a tractor on which he was riding and was run over by the front wheel of an attached trailer. Fractures of the left first rib, both rami of each pubic bone, and an indeterminate injury to the left chest resulted. At the time of injury the patient was in mild shock. There were dullness and absent breath sounds over the left side of the chest and deviation of the trachea to the left. However, hemoptysis, pneumothorax, and emphysema were conspicuously absent. Thoracentesis was performed on one occasion and an unknown quantity of blood removed. Roentgenograms of the chest following injury revealed opacification of the left hemithorax and marked deviation of the trachea and mediastinum to the left (Fig. 1, *A*).

Approximately four months following injury, the patient was given convalescent leave and somewhat later he was discharged from the service with a diagnosis of "atelectasis, left lung."

Physical examination at the time of admission, in 1955, revealed a slender Negro man who breathed easily at rest. The blood pressure was 114 mm. Hg systolic and 80 mm. Hg diastolic. The trachea was deviated to the left and there was flattening of the left chest anteriorly. The apical cardiac impulse was shifted markedly to the left. Breath sounds were absent over the entire left hemithorax except parasternally and paraspinally, where tubular breath sounds were audible.

Routine laboratory studies were reported as normal. Roentgenograms of the chest revealed a marked shift of the trachea and mediastinum to the left and a homogeneous density throughout the left hemithorax (Fig. 1, *B*). A bronchogram disclosed that the left main-stem bronchus ended blindly, approximately 2 cm. distal to the carina (Fig. 2). The right lung was overdistended with a normal bronchial pattern. An electrocardiogram revealed a sinus bradycardia and an incomplete right bundle branch block. Basic pulmonary function studies showed a reduced vital capacity but a normal maximum breathing capacity (Fig. 3). Angiocardiography was performed with 70 per cent Urokon sodium, but the opacity of the left chest precluded good visualization of the vascular bed of the left lung.

On Sept. 19, 1955, operation was performed. After anesthetization but prior to operation, bronchoscopy was carried out and the left main-stem bronchus was observed to end abruptly. The bronchial pouch was lined with normal-appearing mucosa. After bronchoscopy was completed an endotracheal tube was introduced, the patient was placed in the right lateral decubitus position, and the left chest was entered through a standard posterolateral thoracotomy incision, resecting the sixth rib. The left lung was airless and lying free. The heart was almost entirely within the left hemithorax. Pleural surfaces were glistening and normal in appearance. In fact, with the exception of complete collapse of the lung and the abnormal position of the heart, there was no evidence of any morbid process having taken place. The left main bronchus was isolated and an area of complete stricture 1.5 cm. in length was found with a proximal stump of bronchus 2 cm. in length (Fig. 4). The bronchial arteries were not enlarged and the pulmonary artery and veins appeared normal. The distal portion of the stricture was excised and a large amount of clear, gelatinous material was aspirated from the distal bronchial tree (Fig. 5, *A*). It was then possible to inflate the lung easily with slight pressure from a syringe. The region of the carina was dissected next and the proximal bronchial stump amputated above the area of narrowing to gain a normal-sized lumen, free of fibrous reaction. Similarly, a ring of cartilage was excised from the distal end thus producing two lumina of almost equal size. An anterior row of interrupted No. 3-0 silk sutures was first placed, and the sutures were then tied (Fig. 5, *B*). The membranous portion was approximated in a similar fashion, all the knots being tied outside the lumen. Upon completion of the anastomosis, the anesthetist was able to inflate the lung completely without leakage of air at the suture line. It was observed that the left lung was about one third smaller than normal. The left chest was drained with two intercostal catheters and the wound was closed. The patient was then placed in a supine position and a low tracheostomy performed.

The postoperative course was relatively benign. The chest catheters were removed on the second day and the tracheostomy tube on the ninth day after operation. Because of evidence of atelectasis of the left lower lobe, bronchoscopy was performed on the fifteenth day. An 8 mm. Jackson bronchoscope was passed through the anastomosis with ease and a small area of granulation tissue noted on the anteromedial aspect of the suture line. All of the bronchial divisions were patent. A bronchogram performed on the seventeenth day following operation revealed slight narrowing at the suture line although all divisions of the left lung filled (Fig. 6). There was slight dilatation of some of the segmental bronchi but no evidence of true bronchiectatic change. There was also crowding of the bronchi compatible with the decreased volume of the lung. On the nineteenth day following operation the patient was discharged.

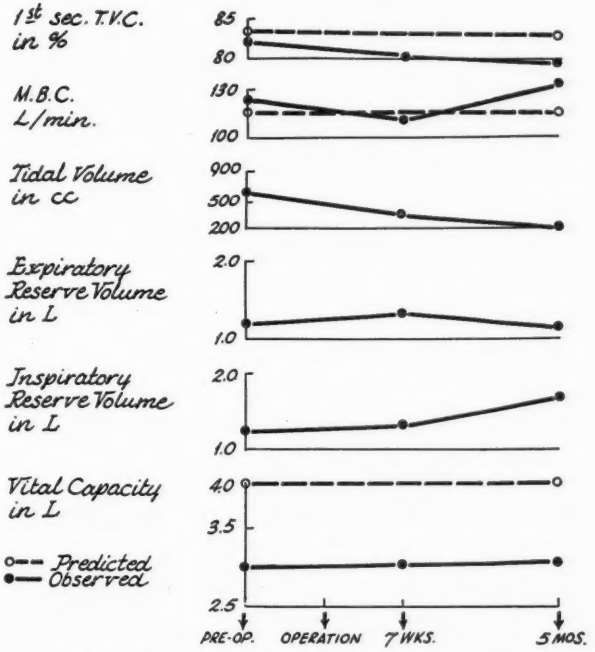


Fig. 3.—Values of basic pulmonary function studies.

He was readmitted for pulmonary function studies at seven weeks and at five months after operation (Fig. 3). At the latter admission, x-rays and bronchography were repeated after the function studies had been obtained and an essentially normal bronchial tree was found with the exception of slight crowding on the left side that was again interpreted as a result of overdistention of the right lung (Fig. 7). The previously noted dilatation of some of the segmental bronchi was no longer apparent.

Since discharge from the hospital the patient has been fully employed as a truck driver. He no longer experiences dyspnea with exercise and is entirely symptom free.

DISCUSSION

Clinical Aspects.—The pattern of injury[2, 16, 29, 41] resulting in rupture of one of the major bronchi is relatively constant. The patient usually sustains

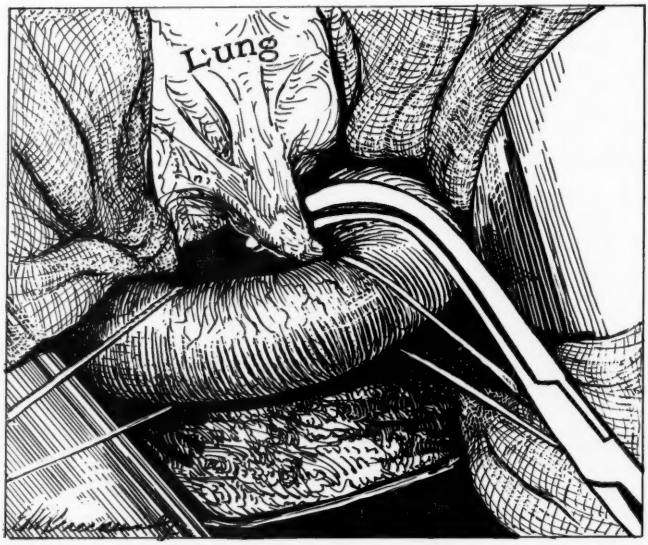


Fig. 4.—Drawing showing the location and extent of the stricture of the left main bronchus. Exposure of the stricture is facilitated by partial mobilization and retraction of the aorta.

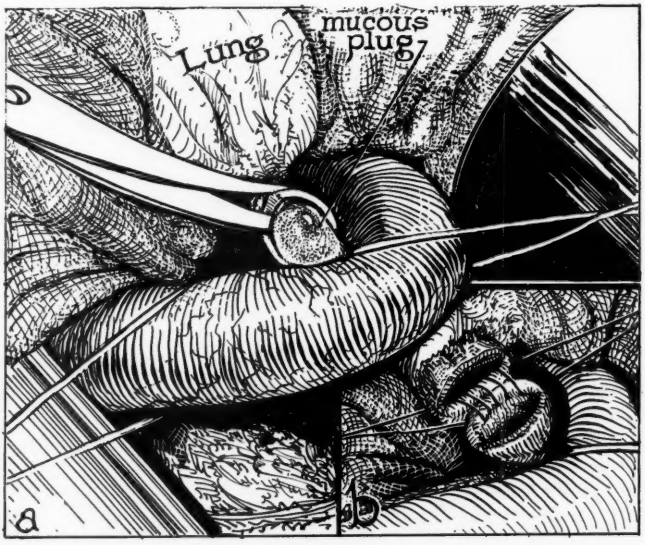
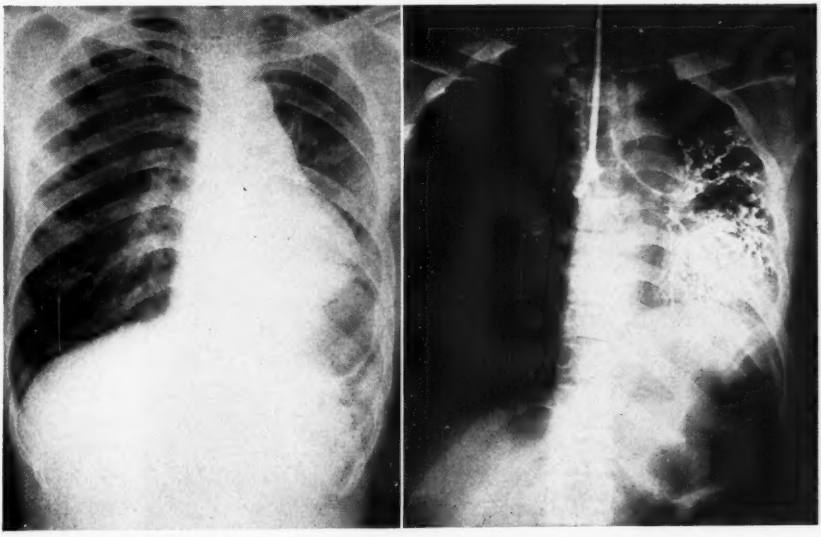


Fig. 5.—*A*, Drawing made at operation showing the gelatinous mucoid material exuding from the distal bronchial lumen after excision of the stricture. *B*, After resection of sufficient bronchial wall to provide a normal lumen, bronchial continuity is restored by end-to-end anastomosis. Simple, interrupted No. 3-0 black silk sutures are tied outside the lumen.

a severe, crushing injury of the chest with the force of injury being transmitted to a closed, hollow viscus.[4] Apparently a shearing type of force is brought to bear on the tracheal bifurcation with resultant rupture of one of the major bronchi.[23] The injury may be confined to the main-stem bronchus,[5, 9, 12, 14, 15, 18, 19, 21-23, 26, 27, 30-32, 34, 35, 38, 39, 43-46, 48] or may extend into the trachea, proximally,[1, 10, 17, 38, 45] or into the secondary bronchi, distally.[10, 11, 13, 23, 25, 37, 39, 42, 45] Hemoptysis, subcutaneous emphysema, and pneumothorax are common clinical manifestations. There may be variable degrees of shock with hypotension and tachycardia. Cyanosis may be a prominent feature. In some instances, other associated injuries bring about the death of the patient before symptoms of bronchial rupture are manifest. However, the majority of patients survive long enough for the diagnosis to be estab-



A. *B.*

Fig. 6.—*A*, Roentgenogram of the chest made approximately two months following operation showing re-expansion of the left lung, but with moderate elevation of the left hemidiaphragm. The mediastinal structures are only slightly displaced to the left.

B, Bronchogram made seventeen days after operation shows a moderate amount of dilatation of the left bronchial tree. There is minimal narrowing at the site of anastomosis.

lished and treatment instituted. The case reported here is very unusual inasmuch as hemoptysis, subcutaneous emphysema, and pneumothorax were not present. Apparently there was complete transection of the bronchus with interposition of the mediastinal tissues so that the rupture was completely sealed. In most of the cases reported, pneumothorax with a persistent, severe air leak is a prominent feature. If the leakage of air is severe enough, early thoracotomy may be required. On the other hand, conservative therapy may be adequate in the early treatment of the lesion and only in the subsequent postinjury period is the true nature of the condition apparent. If bronchial

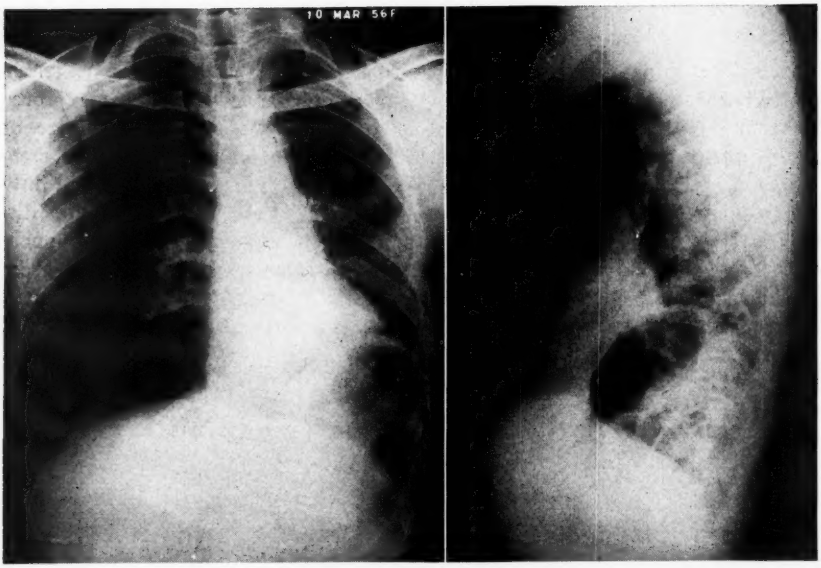


Fig. 7*A*.—Posteroanterior and lateral roentgenograms of the chest made five months after operation show increased expansion of the left lung.

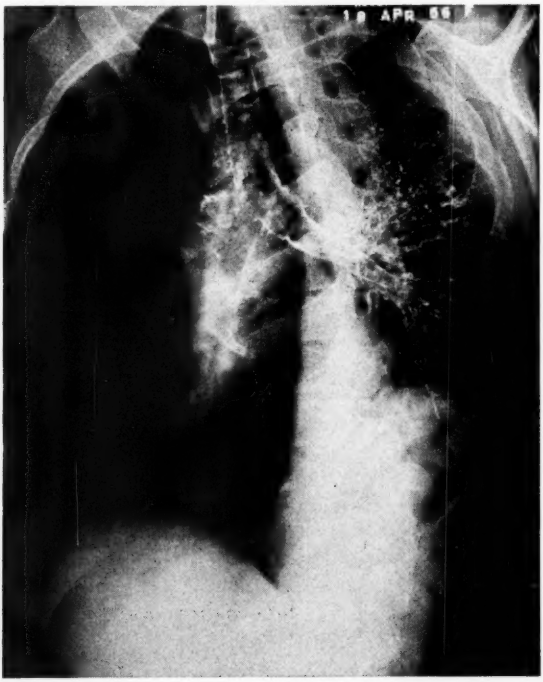


Fig. 7*B*.—In a bronchogram made approximately six months after operation the previously noted dilatations are less apparent although crowding of the bronchial tree is still present. The site of anastomosis can be readily seen.

occlusion is incomplete, repeated infections in the pulmonary tissue distal to the injury almost invariably occur, manifested by pneumonitis or frank suppuration with resultant lung destruction requiring pneumonectomy.[23, 35, 39]

Several aspects of the operative management are worthy of emphasis. Although the prone position has been recommended for optimum exposure of the major bronchi,[3, 36] in this instance, the lateral decubitus position proved eminently satisfactory largely because of the marked mediastinal shift to the involved side. Partial mobilization of the distal aortic arch and the proximal portion of the descending aorta afforded better exposure of the tracheal bifurcation.[3] Following adequate exposure of the area of stenosis, the stricture was completely excised, sacrificing a minimum of normal bronchial wall in order to limit the degree of disproportion. The endotracheal tube was then guided into the right main-stem bronchus with a forceps passed through the proximal stump of the left main bronchus. Thus, positive pressure inflation of the contralateral lung was assured during bronchial repair. The viscid, gelatinous material which filled the bronchi distal to the stricture presented a problem inasmuch as it had to be completely removed before the lung could be re-expanded. It was suggested that one of the detergents be instilled into the bronchus in an attempt to liquefy this material, but aspiration through a small catheter proved successful so this suggested method was not employed. The anastomosis[3, 20, 24] was performed with interrupted simple sutures of black silk since this technique of closure has proved satisfactory for other types of bronchial repair. Tracheostomy was performed primarily as a precautionary measure although it undoubtedly obviated the need for bronchoscopic aspirations during the early postoperative period.

The apparent regression of the previously noted dilatations of the bronchial tree is of interest and adds objective evidence to the studies of Croxatto and Lanari[8] on the pathogenesis of bronchiectasis. They have postulated that complete bronchial obstruction is followed by atelectasis and subsequent "mucous bronchodilatation" secondary to continued secretion of the mucous glands and with the resultant dilatation being directly related to the increased intraluminal pressure rather than the effect of "external stretching." They further postulate that this phenomenon is apparently a reversible one if the factor of secondary infection is not introduced. Although they were unable to show this conclusively in the experimental animal, their hypothesis is nevertheless a valid one. The finding of a bronchial tree distended with mucus has been a constant feature in those cases operated upon several weeks to many years after injury, and histologic sections confirm the impression that inflammation and suppuration are not factors in the usual case of complete bronchial occlusion.[47] The changes noted in the bronchograms after an interval of six months show rather conclusively that this is a reversible phenomenon (Figs. 6 and 7).

Pulmonary Function.—As indicated previously, the mechanism for the production of bronchial rupture and the principles underlying its treatment are well established. On the other hand, little is known regarding the effects on pulmonary function of this injury and its subsequent correction. In re-

porting their experience with a patient operated upon forty-six days following injury, Weisel and Jake[48] described differential pulmonary function studies three months after operation. The injured side was found to have 37.3 per cent of the oxygen consumption, a tidal volume of 249 c.c., a vital capacity of 913 c.c., and a minute volume of 4,980 c.c. These compared with 62.7 per cent oxygen consumption, 300 c.c. tidal volume, 1,826 c.c. vital capacity, and a minute volume of 6,000 c.c. for the uninvolved lung. In a personal communication, the authors state that recent studies indicate an almost equal division of function between the two lungs.[49]

In an attempt to understand the altered physiology associated with this condition, available pulmonary function studies have been utilized. Serial postoperative studies are being done to evaluate the course of the patient from the functional standpoint in addition to the preoperative evaluation.

Methods.—With the patient in a sitting position, subdivisions of lung volume were measured by use of a 9.5 L. spirometer and expressed as volumes at BTPS. Minute ventilation, maximum breathing capacity (MBC), and timed vital capacity (TVC) were then measured. The studies were done preoperatively and at seven weeks and five months postoperatively. At the time of the last study the maximal midexpiratory flow (MMF) of Leuallen and Fowler[28] was obtained. Changes in lung volumes not susceptible to such measures were estimated by the roentgenographic method of Cobb and his associates.[6]

Although absence of bronchial communication to the left lung prevented preoperative bronchospirometry, the procedure has been done postoperatively within two days of the time of determination of total function. A Carlens catheter was used, with proper placement being judged by fluoroscopic position of the catheter, by the absence of transference, and by the change of tracing upon withdrawal. No difficulty was encountered with either catheter passage or placement. The influence of turning the patient from the supine to the right or to the left lateral decubitus position was observed. An unsuccessful attempt was made prior to operation to estimate the distribution of blood in the pulmonary vascular bed by the use of angiocardiography.

Arterial blood was obtained preoperatively and five months postoperatively. Oxygen content, oxygen capacity, oxygen saturation, and carbon dioxide content were measured by the Van Slyke manometric technique. These values are not entirely comparable as the patient was supine and sedated when the initial blood was obtained. At the time the patient was last studied, the response to exercise and inhalation of 100 per cent oxygen was determined. Exercise consisted of stepping up and down on a nine-inch step once every two seconds for three minutes.

The distribution of the inspired breath and volume of dead space was determined five months after operation by the single breath nitrogen washout test.[50]

Results.—The spirometric studies showed a striking lack of variation (Fig. 3). The change in vital capacity and MBC is within the error of the

method. This observed invariance of vital capacity was seen although x-ray examination showed obvious redistribution of air within the chest, as did bronchospirometry. Integrated roentgenographic volumes were consistent with these findings. After operation, the right lung decreased in volume by 800 ml. which is of the same order of magnitude as the 600 to 900 ml. volume present in the left lung at bronchospirometry.

The vital capacity was below its predicted normal in spite of near normal values for TVC and MBC. The resting expiratory level was moderately elevated and has shown no change.

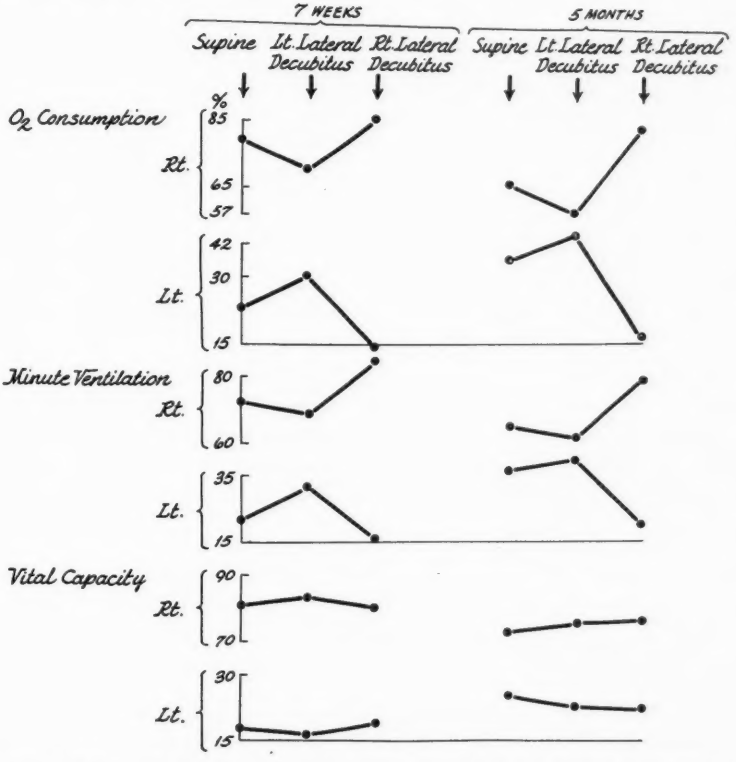


Fig. 8.—Data obtained at bronchospirometry seven weeks and five months after operation.

The addition of the maximal midexpiratory flow (MMF) at the time of last testing falls outside the normal range. This finding is at variance with the one-second TVC and MBC.

With the patient in the supine position, bronchospirometry, seven weeks following operation, showed an oxygen consumption in the left lung of 21 per cent, a minute ventilation of 28 per cent, and a vital capacity of 19 per cent (Fig. 8). Each of the values was slightly increased five months after opera-

tion. When the patient was turned to a lateral decubitus position, the dependent lung had an increased oxygen consumption and a slightly increased minute ventilation while the variation of vital capacity remained within the limit of error of the method (Fig. 9). An interesting shift of the resting expiratory level was observed, the dependent lung having a lower mid-capacity. Furthermore, the shift of mid-position of the two lungs was reciprocally related.

The single breath nitrogen washout test showed a "flat" alveolar plateau. The per cent increase for 500 ml. of expired alveolar gas was less than 1.5 per cent nitrogen. Dead space as determined by the method of Wilson[50] was 100 c.c.

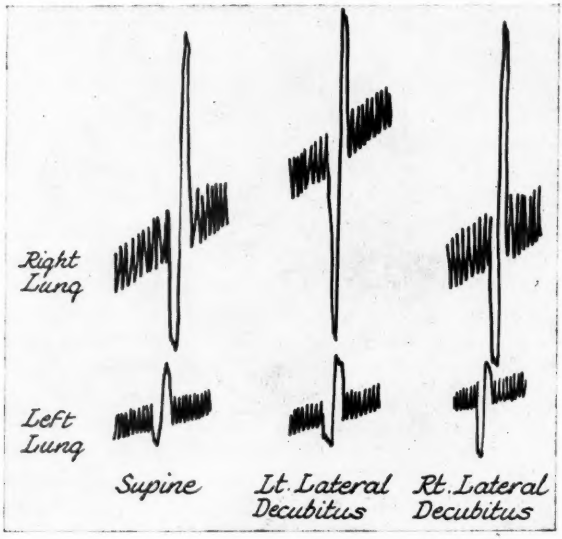


Fig. 9.—Bronchospirometry at five months showing the effect of body position on mid-capacity.

Preoperative blood gas studies at resting conditions showed an oxygen saturation of 94.5 per cent and PCO_2 of 47 mm. Hg. Five months after operation, blood gas studies revealed an O_2 saturation at rest and immediately after exercise of 92 per cent (Fig. 10). After three minutes of inhalation of 100 per cent O_2, the saturation rose to 97 per cent. The step test was performed easily and quickly, and at no time during exercise did the patient develop dyspnea or fatigue.

The most striking finding was the inability of the patient to reach complete saturation following inhalation of 100 per cent oxygen (Fig. 10). The method of Comroe[7] may be used to calculate the amount of shunted blood. As the patient had an oxygen capacity of 18.78 volumes per cent and 2 volumes per cent more oxygen would be present following inhalation of 100 per cent oxygen, the content of blood leaving the pulmonary capillaries was 20.78

volumes per cent. If it was assumed that the mixed venous blood had a content of 5 volumes per cent less oxygen than did arterial blood, then the ratio of shunted blood flow to total blood flow was 37 per cent. A difference of 1 volume per cent from this estimated value gave a range of shunted flow of 33 to 42 per cent.

	Resting	Following Exercise	Following Inhalation 100% O2
Oxygen Content in Vol. %	16.98	16.99	17.85
Oxygen Saturation %	92	92	97
Carbon Dioxide Content in Vol. %	38.77	39.68	33.15

Oxygen capacity was 18.78 Vol. %

Fig. 10.—Blood gas values five months postoperatively.

Comment.—This case represents an extreme alteration of ventilation to blood flow relationship. Physiologically it is opposed to isolated pulmonary artery occlusion with its tendency to hypercapnia and increased dead space for, in the present case, direct measurement showed a normal dead space and an absence of hypercapnia. It demonstrates a low ventilation-perfusion ratio with the effect of a shunt and its tendency to cause anoxia. Failure to reach 100 per cent saturation after 100 per cent oxygen was inhaled is confirmatory evidence supporting the shuntlike effect. The absence of hypercapnia is against general hypoventilation as the cause of anoxia; the failure of saturation to fall with exercise is against a diffusional defect; and the normal single breath nitrogen washout test rules against uneven distribution of the inspired breath.

It was not possible to localize the shunt by available physiologic methods, thus the factors responsible for its development and persistence are not known. However, it appears that several abnormalities resulting from bronchial occlusion may have altered pulmonary circulation. As air volume on the left side decreased, negative intrathoracic pressure increased resulting in overdistention of the right lung. The net effect of this altered pressure relationship may have been to produce a shunt within the pulmonary vascular bed of one or both lungs. Mucus secreting glands, distal to the fracture site, continued to function so that air-containing spaces became fluid-filled spaces.[8] The magnitude of this pressure and its influence on circulation is unknown.

Another important factor may have been development on the left of a closed space filled with fluid which limited volume change to the gas-filled right lung. As exposure to inspired air was lost, the left lung developed a lower oxygen tension which has been shown to decrease blood flow acutely. However, its effect over a period of years is not clear. Finally, changes in bronchial artery circulation may have occurred, although inspection of these structures at the time of surgery revealed no abnormality.

When ventilation of the left lung was re-established, a shunt was present. It is possible that this shunt exists in the right lung, having developed during the long period of increased blood flow through that lung. However, it is more reasonable to assume it is on the left side, either because of localized thickening of the alveolocapillary membrane of sufficient degree to produce a shunt or because there is blood flow to areas as yet not ventilated.

An interesting observation is the shift of mid-position demonstrated at bronchospirometry. This probably represents a compliance change occasioned by change of vascular volume. Whether or not the vascular volumes are more labile than normal is not known.

The decrease of vital capacity would lead to a classification of the ventilation defect as a restrictive one. Curiously enough, the same ventilatory defect persists despite obvious redistribution of gas volumes within the chest cage, and points out the inadequacy of spirometry to give information about the distribution of the inspired breath.

The concepts defined by Otis and his associates[33] may be used to describe the mechanical changes in this case. The spirogram shows a high mid-position probably resulting from increased lung compliance. This change could result from an increase of compliance of one or both lungs. It could also result from a compliance increase on the right side which is greater than a decrease of compliance on the left. It should be remembered, however, that there is evidence for an increased "steady" compliance only, with the effective compliance unmeasured. Theoretically, the right lung which has been overdistended should be more compliant and the left lung, which has been in an extremely small volume for a prolonged period, less compliant. If this variation of compliance exists, a variation of *time constant* between the two lungs may be present resulting in a back-and-forth ("pendelluft") movement of air between the two lungs with uneven pressures applied to the circulation of each lung.

The abnormal MMF may represent a slight increase of resistance to airflow at the site of anastomosis. However, it seems more likely that the increase of compliance with its increase of airway resistance is more likely to be present under test conditions.

One of the most important questions remaining to be answered is whether the increase in oxygen consumption of the left lung, occurring during the first five months after operation, will continue until a normal level is reached. Observation of the patient over a long period of time, with determination of pulmonary function at intervals of six months, is planned in order to demonstrate further the pattern of recovery of lung function.

SUMMARY

1. A case of traumatic rupture of the left-main bronchus secondary to closed trauma to the chest is described.

2. Basic pulmonary function was determined prior to operation and only a decrease of vital capacity was noted.

3. Operation was performed eleven years after the original injury and consisted of excision of the stricture and restoration of bronchial continuity by end-to-end anastomosis.

4. Pulmonary function studies were repeated seven weeks and five months after operation. A progressive increase in function of the previously collapsed lung was observed with a redistribution of vital capacity between the lungs.

5. Bronchography seventeen days after operation revealed moderate bronchiectasis on the left. However, when this examination was repeated about five months later this "mucous bronchodilatation" had disappeared.

6. Blood gas studies disclosed a failure to reach complete saturation after breathing 100 per cent O_2 for three minutes. This is indicative of a "right-to-left" shunt.

7. The progressive improvement in pulmonary function during the first six months after operation suggests that even more recovery of function by the left lung may be anticipated.

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Discussion

DR. JAMES D. HARDY, Jackson, Miss.—We would like to present a similar case which we had about eight months ago.

(Slide) This was a 19-year-old girl who was in a car wreck, sustaining fractures of the left femur, right radius, and both first ribs, plus head injuries. She had a left pneumothorax at the time of injury and a closed drainage tube was put in by the local physician; it was withdrawn three days later and although no expansion of the lung occurred, she had no further respiratory symptoms. This shows the chest film taken at the time of admission to the University Hospital. Note the absence of aeration on the left side.

(Slide) We bronchoscoped the patient and found apparent occlusion of the left main-stem bronchus approximately 3 cm. from the carina, and bronchogram confirmed this impression. I might say that, on the basis of the history and other findings, the possibility of complete traumatic separation of the left main-stem bronchus was suggested by Dr. Watts R. Webb of our department.

(Slide) The left hemithorax was explored with the aid of a double-lumen intratracheal tube. Note the pulmonary artery, the inferior vein, and in the center the distal end of the separated bronchus, with collapsed lung. We attacked the distal end first, snipped off the occluding scar tissue, got a good lumen, and then turned it down to the proximal bronchus which was just adjacent to and behind the aorta. We made no attempt, and no attempt was necessary, to mobilize the aorta.

We took a sterile tube and brought it over the anesthetist's shield and inflated the distal bronchus. The lung inflated readily after the relatively clear greenish mucus had been aspirated from the bronchus. We used No. 4-0 interrupted silk sutures tied inside the bronchus.

(Slide) This shows the patient approximately seven days following operation. Although there was fair expansion of the lung immediately following operation, this improved daily. Moreover, it required several days for the lung field to clear, presumably of retained secretions.

(Slide) This shows the patient ten days following operation.

DR. DONALD L. PAULSON, Dallas, Texas.—Dr. Mahaffey has demonstrated very well the feasibility of restoration of function in an atelectatic lung eleven years after healing of a traumatic rupture by complete occlusion. In our paper on the subject several years ago, we emphasized the fact that all the evidence, clinical and experimental, at that time indicated that these atelectatic lungs secondary to traumatic bronchial rupture, provided complete occlusion had occurred, could be re-expanded if bronchial continuity was restored.

(Slide) This illustrates a case six weeks after injury. The tear has healed by complete occlusion and continuity was restored by means of a dermal graft.

(Slide) This is a similar case six weeks later. Here, as in Dr. Mahaffey's case, pneumothorax was not evident at the time of the original injury. The ends of the severed bronchus were excised and an end-to-end anastomosis was performed.

The problem of acute bronchial rupture of course is divided into acute and chronic phases; the acute phase is far different from the chronic phase; the diagnosis must be made in many instances very quickly; early, if the patient is to survive.

(Slide) This illustrates such a patient with a tension pneumothorax and mediastinal emphysema and subcutaneous emphysema, with a large leak of air through the tubes in the pleural space, in spite of a tracheostomy. The illustration on the right is following repair of the bronchus.

(Slide) This is an illustration of the tear encountered at the time of operation. The diagnosis in these cases may be suspected on the basis of a tension pneumothorax with mediastinal emphysema, frequently in the absence of rib fractures, and may be well demonstrated bronchoscopically. One should be prepared for immediate thoracotomy in

such a case, immediately following bronchoscopic examination. This bronchus was repaired at that time and the patient survived. It is doubtful that such a patient could go on to the chronic phase.

(Slide) This is simply another illustration of a torn bronchus involving the left lower lobe bronchus, as an acute problem.

DR. LYMAN A. BREWER, III, Los Angeles, Calif.—We have all enjoyed this excellent presentation of an extremely well-treated case. These conditions are being recorded with increasing frequency, yet no one's experience with them is very great today. In Los Angeles, we have treated 3 such cases; 2 were long standing, eight and ten years after injury, while the third was of short duration, six weeks after injury. Contrary to the experience of the authors, we were unable to re-expand the lungs on the affected sides in the two long-standing cases. This was due to fibrosis and cystic changes in the lung, which made the lung nonexpansile even though it was possible to restore the airway adequately. Subsequent pathologic examinations on these lungs were similar to chronic fibrosis, cystic change, bronchiectasis, such as one sees in chronic obstruction of the bronchus from other causes.

I think this poses an extremely interesting problem. Why did our long-standing cases show these chronic inflammatory changes and why, in the case reported today and some in the literature, was the pulmonary tissue relatively uninvolved? The basic factors are worth our consideration. We derived the impression that secondary infection in the lung probably was one of the most important basic reasons although one might consider extensive intrapulmonary hemorrhage, previous disease or impairment of the blood supply of the lung as other factors. But it seemed, in reviewing our cases, that infection was the primary factor. In the patient of six weeks' duration, pulmonary infection was controlled with antibiotics and we were able to repair the bronchus successfully and get an adequate expansion of the lung, while in our cases of long-standing complete traumatic rupture of the bronchus, no antibiotics had been used. Therefore, in the management of acute rupture of the bronchus if immediate surgery is not available, control of infection is probably one of the most important factors in addition to the other measures fundamental to the management of trauma.

DR. VICTOR H. KAUNITZ, Buffalo, N. Y.—Dr. Mahaffey and his group have shown a very excellent result in a well-studied case. I would like to present briefly a similar experience in which the outcome was not so fortunate, although the patient is fine now.

A 19-year-old girl, the driver of an automobile in a severe accident, sustained bilateral upper anterior rib fractures and bilateral pneumothorax. (Slide) This was treated within twenty-four hours by bilateral catheter drainage and both lungs re-expanded promptly.

(Slide) However, over the next few days there was progressive opacification of the left chest. The initial drainage from the left catheter had been bloody and we assumed we were dealing with a traumatic left hemothorax, but the patient ended up with complete opacification of the left chest.

The patient at this time was completely well, afebrile, and had been on continuous large doses of antibiotics. One month later she was transferred to our hospital in Buffalo from the rural hospital to which she had been admitted, for planned decortication. However, preliminary bronchoscopy showed complete obliteration of the left main bronchus at the level of the carina. We passed a small bougie through this, which I would not recommend, and then performed a bronchogram, passing a small catheter through this obliterated portion.

(Slide) Much to our surprise, the catheter was found to lie in the mediastinum and there was Lipiodol in the right pleural cavity. We also produced a very small right pneumothorax. The patient, however, had no difficulty from this and a few days later we went ahead with the planned left thoracotomy. After prolonged dissecting we were unable to visualize the proximal end of the left bronchus, nor could the anesthetist with

gentle positive pressure expel any gas through it. There was considerable suppuration in the distal left main bronchus, and the only recourse was to perform a left pneumonectomy, which was done. The patient had an uneventful postoperative course and now, three years later, is quite well.

DR. THEODORE R. HUDSON, Chicago, Ill.—I would like to say that Dr. Mahaffey's recital is a tribute not only to the surgeon's skill but also to the staying power of the lung concerned.

(Slide) In spite of the fact that Dr. Mahaffey's patient and another one mentioned here today did not have a pneumothorax, I suggest that this problem of ruptured bronchus is primarily one of tension pneumothorax. The girl whose chest x-ray you seen in the slide was severely injured in a steering wheel accident and, as you see, has practically complete collapse of the right lung with severe subcutaneous emphysema. The needle you see in the lower part of the chest was put in by a surgical resident, in the wrong place obviously, but nevertheless I am convinced that it was lifesaving. This girl was operated on a few hours after the injury with a diagnosis of ruptured bronchus and at operation she was found to have the right primary bronchus completely avulsed from the trachea at the carina, with loss of one complete ring of the primary bronchus. The bronchus was anastomosed to the trachea by simple suture as has been described in the cases discussed previously.

(Slide) This shows her condition now with a fully expanded and well-functioning lung. I would suggest that as a group we could afford to be a little more aggressive when it comes to dealing with tension pneumothorax, particularly following chest injury, and especially if subcutaneous or mediastinal emphysema can be demonstrated. In this way we will not only save lives but will be spared the much more difficult surgical problems similar to the one presented in Dr. Mahaffey's very excellent paper.

DR. RICHARD M. PETERS, Chapel Hill, N. C.—I will address my remarks to the problem of the shunt in these cases. We have done some work on atelectasis in this regard. There is a marked decrease in blood flow to the lung following atelectasis. This decrease in flow is not due, apparently, to the explanation which Dr. Liebow and his group have put forward, namely, an hypertrophy of the bronchial arterial system causing back pressure and preventing a shunt, because if there is no infection in these lungs there is no hypertrophy of the bronchial arterial system. This has been shown in a number of dogs, and I would like to suggest that this might answer Dr. Brewer's problem of how to determine whether one of these lungs is significantly damaged by infection. If there is an hypertrophy of the bronchial arterial system which is seen in bronchiectasis, tuberculosis, etc., it may be likely that there has been considerable damage from infection in the lung. If the bronchial arterial system, after dissecting the bronchus out, is normal, I think one can assume that there probably has been very little infection in the lung.

The shunts which you see here I am sure are in the range of flows seen during atelectasis in experimental animals and in human beings. It amounts to from 20 to 30 per cent of the cardiac output.

DR. DE WITT C. DAUGHTRY, Miami, Fla.—The patient, presented in our case last year, with fracture of the trachea and the right stem bronchus is continuing to do well, and I arise at this time to present a serious traumatic problem representing a little different type bronchial interruption. To my knowledge this is the second case of traumatic torsion of the lung to be presented and is the only one in which the patient survived surgery. The immediate and subsequent course was confusing but most interesting.

A 7-year-old girl was admitted to the hospital following a crushing injury to the left lower chest. She sustained a fracture of the left femur, several rib fractures on the left, and a ruptured spleen. A splenectomy was performed. The initial x-ray of the thorax showed some apparent congestion or early atelectatic changes in the left upper lobe. The x-ray changes in a few hours progressed to complete opacification of the left lung field associated with absence of breath sounds. There was no hemoptysis and no blood could be as-

pirated from the left pleural space. Mild fever, elevated white blood count, and malaise persisted. Forty-one days following injury she was operated upon with a preoperative diagnosis of an organizing, clotted hemothorax. She was found to have a 180 degree clockwise rotation or torsion of the left lung with gangrene of all the lung except the superior segment. It was felt at the time of surgery that the viable superior segment in a 7-year-old child might serve a good purpose. The other segments of the lung were excised.

(Slide) This shows the vascular pattern in the left lung radiating upward and laterally rather than downward as you see on the opposite side. This is the diagnostic sign that should, in the future, lead us to the diagnosis in its early reversible stage. The next x-ray shows complete opacification of the left lung within a period of eight or ten hours. The third x-ray, some thirty-six or thirty-eight days after injury, reveals breakdown of lung parenchyma producing free air pockets or essentially multiple bronchopleural fistulas. Multiple rib fractures over the left lower thorax are demonstrated.

This color photograph taken at the time of surgery shows the one viable segment lying next to the heart which is, of course, an abnormal location for this segment. The remainder of the lung is gangrenous and one can visualize the loss of lung tissue in these areas representing abscess and bronchopleural fistulas. The next color photograph represents the necrotic segments of the lung which were excised. The color photograph shown here reveals the well-aerated superior segment of the lower lobe after reduction of the torsion and return of it to its normal location.

This composite slide of the immediate postinjury x-ray and the x-ray six weeks following surgery reveals a little more clearly the abnormal vascular pattern radiating superiorly and laterally, and how adequately the remaining superior segment has filled the left thorax.

A more detailed report of this case, including follow-up pulmonary function studies, will appear later.

DR. BENSON B. ROE, San Francisco, Calif.—I have no slides to show, but we have 2 cases of bronchial reconstruction, both for inflammatory disease, which is indeed a different problem. I think, however, a certain principle of bronchial reconstruction is worthy of bringing to light in this regard. I expected that Dr. Gebauer would be here and would have this to say for himself, but I know that he has emphasized the importance of the suture material used in circumferential bronchial reconstruction. It has been well shown histologically that silk does produce enough inflammatory foreign body reaction to redevelop stricture, which happened in one case which I did after seventeen months, although the original bronchograms at three months showed the lumen of the lobar bronchus to be wide open. The use of stainless steel wire may avoid this late complication.

DR. J. L. EHRENHAFT, Iowa City, Iowa.—We have had experience recently with 4 patients who had suffered crushing injuries to the chest resulting in lacerations or complete transections of the trachea or either of the main stem bronchi. Two of the patients arrived at the hospital moribund and died shortly after admission. At post-mortem examination, one patient revealed a small laceration of the trachea above the carina while the other revealed a transection of the right main-stem bronchus extending up into the trachea. Those 2 patient arrived too late for any further help.

We did operate on 2 patients. One young man was admitted forty-eight hours after an automobile accident. He was in extremis when first seen but rapid investigation established the diagnosis of a transection of the right main-stem bronchus. At the time of emergency right thoracotomy, it was found that the azygos vein was lacerated and that there was complete transection of the right main-stem bronchus and a tear extending into the trachea. This lesion was repaired. This slide shows the chest roentgenogram prior to repair and this slide shows the chest roentgenogram after repair of this bronchus. Note the complete expansion of the right lung. Four months after repair of this lesion

the patient returned with a completely atelectatic right lung resulting from a stricture at the site of the bronchus repair. Re-exploration revealed the lesion to be such that reconstruction of the bronchus was not feasible.

The fourth patient suffered injuries in a tractor accident, which crushed her chest and also caused fracture of the left clavicle. We saw the patient six months after the injury and on physical examination and further investigation it became obvious that there was a transection of the left main-stem bronchus. The anatomic situation and the repair in this patient was very similar to the one shown by Dr. Mahaffey. The slides demonstrate the lesion prior to and after repair of the left main bronchus. The bronchograms outline the area of reconstruction of the left main bronchus very well. The patient at the present time is perfectly well with a normally functioning left lung.

These types of injuries seem to be on the increase now; many of them are the result of crushing chest injuries suffered by drivers of automobiles—steering wheel injuries.

DR. PAUL C. SAMSON, Lafayette, Calif.—I have listened to this presentation with great interest and appreciate the essayist's reference to the case briefly reported before this Association two years ago by Byron Evans. I believe it will be of interest to bring you up to date. This patient is unique on three counts. His successful bronchial anastomosis was performed fifteen years following the bronchial transection, which is the longest period known to us. Second, the injury occurred at one year of age and the repair at age 16. This gave us an opportunity to observe an "infant" lung in an adolescent, since apparently there was little or no growth of the lung while it was functionless. Third, this operation was performed nearly three years ago and it is, therefore, one of the early group of successful repairs for this type of injury.

At present this young man has no objective symptoms of pulmonary dysfunction. He engages in all types of athletics without difficulty. There has been progressive improvement in timed vital capacity and in maximum breathing capacity as follows: VC (1954), 1,925 c.c.; (1955) 2,300 c.c.; (1956) 3,650 c.c. MBC (1954), 72 L. per minute; (1955) 90 L. per minute; (1956) 134 L. per minute. X-rays show the right lung to remain small, but there has been no relative change in the volumes of the right and left lung over the past three years. The right diaphragm is still elevated and paradoxical. The bronchograms show good segmental filling without atelectasis or bronchiectasis. The ventilatory capacity of the right lung is over one half that of the left. However, the oxygen consumption is less efficient and is only one fifth that of the left lung.

I believe it is fair to assume that there must be some hyperplasia of the lung in response to the stimulus of use but, of course, there is no laboratory proof of this. In any event, the patient has benefited greatly from his operation and there seems to be no question of the validity of the concepts that with complete traumatic transection, infection will *not* supervene; and that successful repair with a resultant usable lung may be performed many years after injury.

DR. OSCAR CREECH, JR., Houston, Texas (Closing).—We wish to thank the discussants for their remarks, and would like to emphasize that the two important features of this case are, one, the fact that although the left lung was re-expanded, there was no alteration in vital capacity; there was simply redistribution of inspired air. Second, and more important, the failure of the patient to reach complete saturation of the arterial blood following breathing 100 per cent oxygen indicated a shunt of pulmonary blood flow of about 35 per cent. This has shown a tendency to decrease with time and we feel that this test will provide the best criterion of recovery of lung function.

CONGENITAL ATRESIA OF ESOPHAGUS

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ALTHOUGH the pathologic anatomy of congenital atresia of the esophagus with tracheoesophageal fistula was known to pathologists as a rare and fatal curiosity for over two centuries,[1] clinicians did not become interested in making the diagnosis until thirty years ago, and development of effective treatment by surgeons occurred only in the last decade. The embryology, etiology, and incidence of the anomaly and its relationship to accidents of gestation and association with other anomalies are still uncertain. With a few notable exceptions, most of the increasingly numerous papers on the subject are concerned largely with reports of isolated cases, with various techniques of surgical management, or with series collected from such reports. It has seemed desirable, therefore, to collect and to summarize the record in a single center where a considerable experience has accumulated.

This report deals with 136 cases of congenital esophageal atresia with and without fistula seen at Babies Hospital or born in Sloane Hospital, both now units in the Columbia-Presbyterian Medical Center in New York, in the half century between 1903 and 1953. The majority of the patients have been seen, and most of these personally cared for by the authors, 27 having been previously reported.[2] The present series includes 101 patients who were operated upon, 32 of whom survived operation and 29 of whom were living and well at the time of this review.

EARLY DIAGNOSIS AND TREATMENT

The evolution of diagnosis and treatment in the group here reported is representative of the general experience with this anomaly. In the first 4 cases seen, in 2 of which attempts to pass a catheter into the stomach failed, attention was directed primarily to the esophageal atresia, though a note was made in one that "regurgitation of formula through the nose is suggestive of the presence of fistula." All were treated by gastrostomy only, and died of sepsis and pneumonia. Because of these discouraging results, the next 6 patients were not operated upon, and all died of pneumonia in the first week of life. This was the total experience in the first twenty years of the half century.

In 1923, diagnosis by x-ray was first carried out. The first x-ray was reported as demonstrating "congenital atelectasis." Following autopsy dem-

Read at the Thirty-sixth Annual Meeting of The American Association for Thoracic Surgery at Miami Beach, Fla., May 7 to 9, 1956.

onstration of the true nature of this unoperated infant's anomaly, a second case in the same year was diagnosed by contrast medium and an attempt was made to correct it surgically. In this procedure, Dr. Bolling not only performed a gastrostomy but also ligated the esophagus intraperitoneally. The ligature cut through and the infant died of peritonitis.

There followed a period in which x-ray diagnosis became increasingly accurate, but surgery was attempted only when no fistula was recognized. Of the next 12 patients, 9 were diagnosed during life and 3 were treated by gastrostomy, all dying of aspiration shortly thereafter.

In 1941, Dr. E. J. Donovan performed transpleural ligation of the lower esophageal segment and gastrostomy on 2 infants. In both, death followed cutting through of the ligatures. In the same year, Drs. W. G. Heeks and Hogg attempted a direct end-to-end anastomosis of the esophagus through a right retropleural approach, after dividing and ligating the fistula. Unfortunately, this operation, now the procedure of choice, failed through breakdown of the anastomosis, as did two subsequent ones performed the same year. One of these babies survived for two weeks, however, and gave encouragement to the concept that this condition might not necessarily be hopeless, although no survivor had yet been reported.

In the following year, 1942, an infant survived following division and closure of the fistula, cervical esophagostomy, and subsequent gastrostomy as described by Humphreys.[2] This procedure, essentially similar to successful operations previously performed by Leven[3] and Ladd,[4] was carried out in 4 more cases the same year, with 3 survivors of the 5. The first patient is now living and well, swallowing normally through a subsequently reconstructed esophagus, but the other 2 ultimately died of later complications.

In 1943, the first successful case of direct anastomosis in this series was performed shortly after a survivor of this procedure was reported by Haight and Towsley.[5] Since that time a direct anastomosis has been done whenever possible, cervical stoma and ligation being done only eight times in the seventy-nine operations performed in the next ten years.

Over the course of the early years of recognition of the anomaly and the attempts to correct it, it is interesting to note how cases tend to appear in groups. Recognition of one case apparently stimulated awareness of the condition, with the result that other cases were recognized within short periods of time, after which the characteristic symptoms appear to have been forgotten and cases perhaps missed for a time until another one was recognized. This phenomenon is apparent even in later years. In our own institution, cases occasionally are discovered at autopsy which were not recognized clinically. This emphasizes the importance of alertness to the possible presence of this defect and its characteristic symptoms in making the prompt diagnosis on which effective treatment depends.

CLINICAL DATA

The occurrence of this anomaly as seen at the Babies and Sloane Hospitals over this 50-year period is shown by 5-year periods in Table I. With

TABLE I. BABIES AND SLOANE HOSPITALS, TOTAL CASES—1903 THROUGH 1952

	NUMBER OF CASES
1903-07	1
1908-12	2
1913-17	4
1918-22	2
1923-27	8
1928-32	9
1933-37	7
1938-42	14
1943-47	37
1948-52	52
Total	136

recognition at the beginning of the last decade that successful operative treatment was possible,[2-5] there is a rapid increase in numbers seen. The conclusion seems inescapable that the defect is not as infrequent as the earlier experience implies, but that it either was unrecognized, or that little effort was made to treat it in the earlier period because of the apparent hopelessness of the situation. It is probable that the incidence has not changed, being about one in 3,000 births in the group from the Sloane Hospital included in this series, but in the past the anomaly was often overlooked and death ascribed to neonatal asphyxia, atelectasis, or aspiration pneumonia.

Increased awareness of the condition, as evidenced by an increasingly early age at the time of admission to the hospital is shown in Table II, which

TABLE II. BABIES HOSPITAL CASES 1903-52
(STILLBORN, NEONATAL, AND AUTOPSY DIAGNOSED EXCLUDED)

	NUMBER OF CASES	AGE ADMITTED	AGE DIAGNOSED	NUMBER OPERATED UPON	NUMBER OF SURVIVORS	PER CENT OF SURVIVORS
1903-21	9	5.5	?	4	0	
1922-31	11	4.7	5.2	3	0	
1932-41	10	2.8	2.9	6	1	
1942-43	12	4.3	3.5	11	5	45
1944-45	14	4.0	4.1	13	1	8
1946-47	16	3.2	2.9	16	4	25
1948-49	19	2.7	2.5	18	7	39
1950-51	18	2.1	2.1	18	7	39
1952	12	2.0	2.0	12	8	66
Total	121	3.6	3.3	101	33	

also shows an increasingly early age at which the diagnosis was made, especially in recent years. In general, delay in diagnosis and admission for treatment in the earlier group resulted in the children's being in less good condition due to dehydration and aspiration pneumonia, with correspondingly lower admission weights and higher mortality. The burden of early recognition falls largely on the obstetrician, the pediatrician, and the nursing personnel of the newborn nursery. If they are suspicious in regard to any child who has excess mucus, episodes of cyanosis, and who does not properly take fluid in the newborn period, more of these cases will be recognized earlier than at present, before a great deal of aspiration has occurred. There is no real

substitute for awareness and careful, accurate observation. In many of the infants in this series, the nurses' notes had the diagnosis in them, whereas the medical histories did not.

Neither the clinical history, nor the physical findings have changed since the often quoted classical description given by Gibson[1] in 1703. Yet, in some of the old charts in this series before the defect was well known, many erroneous speculations were indulged in as to the nature of the anomaly. An important clinical observation is that the regurgitation or vomiting or coughing, as it might be more accurately described, of bile in these cases should not lead one astray and bring the question of intestinal obstruction too strongly to the fore. A number of these cases did reveal this type of history. In a few it was a reflection of intestinal obstruction at some other point in the gastrointestinal tract, but in most this was not so. One of the latter cases actually had been operated on at another hospital for intestinal obstruction prior to admission to Babies Hospital.

Although the diagnosis may frequently be made on history alone, physical signs and x-ray examination are usually necessary to confirm it. Almost all show signs of atelectasis or aspiration pneumonia, characteristically in the right upper lobe. Obstruction to the passage of a catheter through the esophagus, especially demonstration of its turning back upward into the pharynx on x-ray or fluoroscopy, may be sufficient and was often used in the earlier cases. Later, x-ray demonstration of the anomaly following a swallow of barium was frequently used. Although this delineates the lesion well, by 1941 it was realized that aspiration of barium into the lungs frequently resulted, and instillation of a few drops of radio-opaque oil with prompt aspiration after obtaining roentgenograms was substituted. This is useful in demonstrating the size and level of the upper pouch and often demonstrates also the presence and site of the fistula.

The presence of air in the gastrointestinal tract is clear-cut evidence of the presence of fistula between the tracheobronchial tree and the lower segment. Its absence, however, though suggestive, is not a sure sign of the absence of such a fistula. In one instance, lack of air in the stomach at two days, and in another at seven, led in the early period to this erroneous assumption. In each case, gastrostomy without closure of the fistula resulted in fatal aspiration of formula. Occasionally the lower esophageal segment may be demonstrated on lateral roentgenogram by the presence of air in it. Fistulas between the upper pouch and the trachea are usually impossible to demonstrate except by operative dissection.

EMBRYOLOGY

The type of anomaly in this series follows closely the experience of others, 122, or 90 per cent, being the 3b type of Vogt.[6] In this, the esophagus ends in a blind pouch high in the posterior mediastinum, and the lower segment originates in a fistula from the membranous portion of the trachea, the carina, or one of the primary bronchi. All but two of the recoveries fall in this group.

There were three instances of double fistula, in two of these the upper fistula was pharyngotracheal, entering the trachea just below the larynx. In another, there was an atresia with fistula and no lower esophagus. There was one stenosis of the esophagus with no fistula, and 8 cases of atresia with no

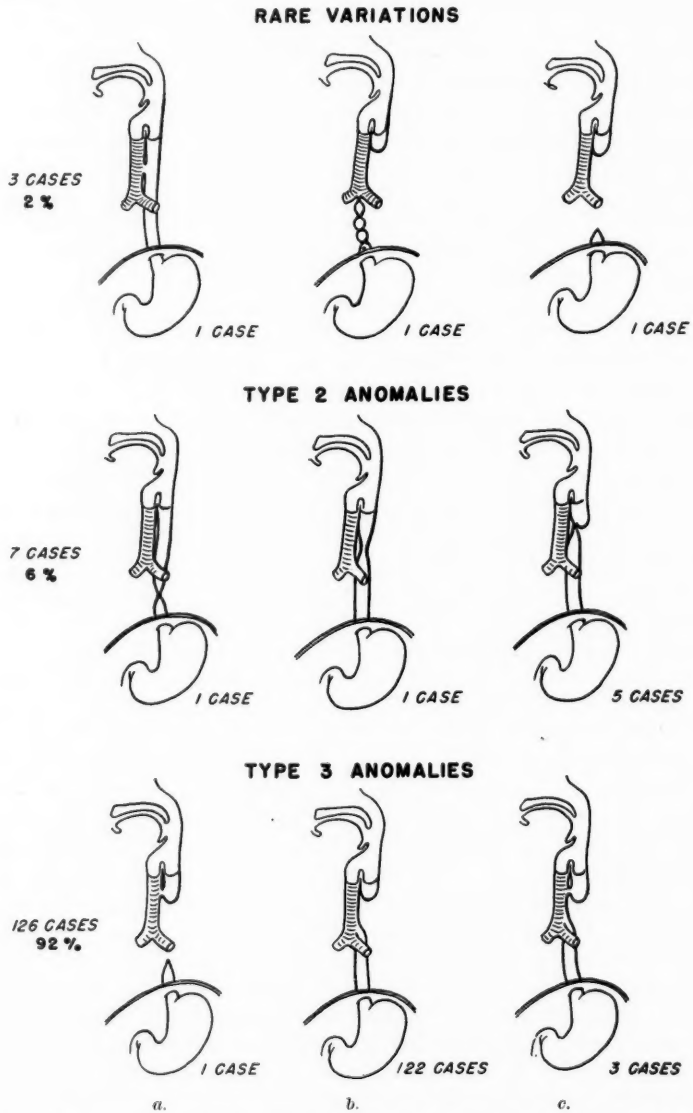

Fig. 1.—A diagram to show the types of anomaly encountered with figures illustrating numerical frequency of each. Ninety-two per cent were Type 3 anomalies; Type 3b in 90 per cent.

fistula, one with no lower esophageal segment, and the others with the lower segment present in varying lengths from one to several centimeters. In one of these cases, the lower esophagus consisted of multiple cysts joined by fibromuscular bands to one another and joining the trachea in the usual position just above the carina. In another case, the proximal point of atresia lay at the level of the eighth thoracic vertebra and extended distally for 1.5 cm. as a fibromuscular band, where the esophagus again became patent and normal in size. Finally, there was one case of fistula without stenosis (Fig. 1).

The etiology and the abnormal embryology of this defect have been the subject of considerable discussion. It seems probable that an incomplete cleavage between trachea and esophagus, together with the failure of recanalization of the esophagus, will explain all of the types of the anomaly. Complete transection without a discernible trace of connection to the trachea or lower esophagus has been seen occasionally in these cases, as is also seen in atresias of the small bowel, but the more usual finding is a persisting fibrous or fibromuscular band or multiple cysts making connection with the distal portion of the esophagus.

ASSOCIATED ANOMALIES

Of the total group of 136 patients, 75 are known to have had other congenital malformations. Among the 104 who died, 93 were examined at autopsy and 61 of these showed other anomalies; of the remaining 11 who were not autopsied, 5 showed gross associated anomalies. Thus, two-thirds of the infants who died were handicapped by other malformations. In contrast, among the 33 survivors only 9, or less than one-third, showed other anomalies and only one of these, a tetralogy of Fallot, was of sufficient severity to result fatally at an older age. The remainder are for the most part of minor nature such as hernia or hemivertebra.

FACTORS INFLUENCING SURVIVAL

Prematurity or low birth weight is a factor which adds to the risk of any surgery in the neonatal period. It is interesting to determine how these related factors have influenced the results in this series. Of the entire group 27 were listed as premature, 34 as full term, and in the remaining 75, the relation of the birth to expected term was not stated or not clear to the parents. The stated maturity, therefore, is of little help in relation to survival. More significant in relation to maturity is the birth weight. Of the entire group, birth weight was recorded in 125. The distribution among these in 500-gram groups is shown in Fig. 2, which also shows the corresponding weights among those which were born dead or died in the first day of life, in contrast to those who survived. As might be expected, deaths at or within twenty-four hours of birth were highest in the small and presumably premature babies, whereas the largest number (68 per cent) of survivors fall in the weight range from 2,500 to 3,000 grams. This is also the peak of birth weight range for the entire group and falls into the slightly premature or small full-term range. Although no child under 1,800 grams survived, it is

interesting to note that three definitely premature infants of 1,800, 1,818 and 1,900 grams did survive operation and are now well. Thus, it appears that prematurity as judged by weight, though a determining factor at the lower extreme of size, does not preclude survival.

It is generally agreed that delay in making the diagnosis adds to mortality, largely because of the inevitable onset of aspiration pneumonia, especially if attempts are made to feed the baby. In the infants who survived more than one day but were not operated upon, the average age at death was 6.7 days, the longest survival being 18 days. Of the operated group, the average age at operation in the survivors was under 4 days, as contrasted with over 4 in those who did not survive. This is questionably a significant difference.

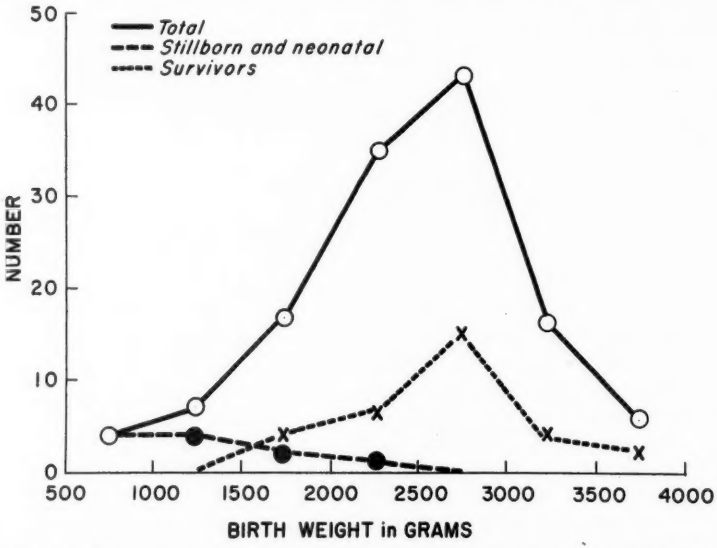

Fig. 2.—Birth weight distribution. Chart to show frequency by birth weight in 500-gram groups, of total group, the neonatal or stillborn group, and the group of survivors. The peak in total number and in survivor percentage falls in the 2,500- to 3,000-gram range. Below 1,500 grams, there are no survivors and the majority die at birth or within twenty-four hours.

In recent years, however, with earlier recognition, some delay has been deliberately introduced in preparing the baby for surgery so the groups are not strictly comparable. It remains our impression that mortality is less if the operation is done as soon as possible after birth.

The preoperative care of these patients is important. On admission and after diagnostic procedures have been completed, the child is placed on nothing by mouth, put in an incubator with the temperature controlled and additional moist oxygen, and continuous nursing care is provided. The pharynx is suctioned every one-half hour with a small soft rubber catheter, the head of the incubator platform is slightly depressed, and blood to the amount of 15 to 20 c.c. per pound of body weight is made ready to go to the operating room. Infants who are jaundiced receive vitamin K preoperatively,

and hydration is achieved by the use of a polyethylene intravenous catheter with a continuous drip of 5 per cent dextrose. Since these children are easily overhydrated, fluids in general do not exceed 75 c.c. per kilogram per day, of which only 75 c.c. or less is saline solution, the remainder being 5 per cent dextrose. It is no longer felt that operation should be done immediately as an emergency. Sufficient time, up to twenty-four hours, should be taken to restore hydration, give antibiotics, and restore pulmonary aeration by careful frequent aspiration. This will usually result in the infants' being better able to withstand operation than if operated on immediately after admission to the hospital.

The operative procedure has changed over the years. In the early group, gastrostomy only, with open drop ether, was uniformly fatal. Gastrostomy as a primary procedure is now reserved for the rare case at which there is reasonable certainty that a fistula does not exist. In the past ten years, this was carried out in 2 patients, one of whom survived and was found two years later to have a short segment of atresia. Successful resection of this segment and end-to-end anastomosis was then done. The other patient, who had no lower esophageal segment, succumbed to pneumonia thirty-two days after gastrostomy and thoracic exploration. The first survivals in the group here described were treated by retropleural divison and closure of the fistula and cervical esophagostomy under local anesthesia.[2] This method has the disadvantage of the need for feeding by gastrostomy for a long period and eventual reoperation to restore esophageal continuity. It is now reserved for the few cases in which the esophageal ends are so widely separated that they cannot be approximated without dangerous tension.

Since its first successful accomplishment in 1943, direct anastomosis has been the procedure of choice. If the infant is large enough, intratracheal anesthesia, usually cyclopropane, is used. Positive pressure with face mask only is preferable if the glottis does not readily admit a tube, and local anesthesia is still used in preference to inhalation anesthesia if the infant is very small or if there is much accompanying pneumonia. A right retropleural approach is preferred. Until 1946, a single layer anastomosis was done; since that time a two-layer technique as described by Haight has been used in most cases. In achieving a high percentage of anastomosis, even covering gaps of 2 or 3 cm., the following points are important. Dissection of the upper pouch high into the neck should be extensive, and painstaking, and complete separation of the pouch from the trachea, to which it is often densely adherent over a fairly long interval, should be accomplished. The fistula usually is approached first. It is separated from the trachea by a clean incision and the opening in the posterior wall of the trachea sutured with interrupted fine silk. This gives the anesthetist better conditions and obviates increased distention of the stomach. After the muscularis has been dissected from the mucosal portion of the upper pouch, the latter is brought down and sutured at appropriate points to the opening in the lower esophagus, which can be enlarged to an adequate size if necessary before opening the mucosal pouch of the upper segment. After it is once anchored, then the upper pouch is

opened and the anastomosis completed, using all layers of the lower segment. The cuff of muscularis from the upper pouch is then drawn downward over the inner suture line and sutured to the muscularis of the lower segment. Fine interrupted sutures are used to avoid constriction at the line of anastomosis.

Other methods have been attempted which have proved less satisfactory. Because esophagogastric anastomoses in adults are usually done through a left transpleural approach, it seemed reasonable to attempt an analogous operation in a number of these infants. Three esophagogastrostomies all resulted in death in the immediate postoperative period. Although other surgeons have reported recovery following this procedure, it appears to be definitely more shocking, and presents difficult later feeding problems. Eleven anastomoses of the esophagus were done through the left pleural cavity. Technically, this method has some advantages but our results suggest that leakage from the anastomosis is more likely to follow, especially if it is made lateral to the aortic arch, and mortality was definitely higher in this group. The method has therefore been abandoned.

During operation, blood is given to replace that lost, taking care to avoid excessive blood or fluid replacement. Inevitable contamination of the mediastinum from the open esophagus and trachea has been counteracted with local antibiotic (sulfadiazine in the earlier cases, recently streptomycin-sulfamylon solution). Leakage from the anastomosis or tracheal closure is carefully checked by raising intratracheal pressure with the mediastinum flooded with saline solution. Some of the earlier patients were drained but it is now considered inadvisable and unnecessary to do so, even if the pleura is inadvertently opened, but special care is taken to be certain that the lung is fully expanded when the chest is closed.

Postoperatively, the infant is returned to moistened and oxygen enriched atmosphere under constant nursing surveillance. Frequent pharyngeal aspiration is continued, but a catheter is not left in the esophagus. Carefully controlled intravenous fluid therapy is continued and no oral feedings are given for a variable period up to ten days. If the anastomosis has been a very satisfactory one, and if it appears that the infant has begun swallowing saliva without difficulty, careful feeding in small amounts may be begun in the second week. Usually it is more expedient to perform a Witzel gastrostomy under local anesthesia from two to four days after the first procedure and to begin small feedings through this a day or two later. By ten days, the gastrostomy feeding may be increased to an adequate caloric and vitamin content. The status of the anastomosis may then be determined by roentgenogram following a small swallow of barium. An increasing amount of formula is then given by mouth, and a correspondingly decreasing amount by gastrostomy until by the second or third week gastrostomy feeding may be discontinued. Before removing the gastrostomy tube, a month or more after operation, the anastomosis should again be examined by x-ray, since late stricture may occur. The first patient to survive anastomosis required retro-

grade dilatation at intervals for a year, but now shows no evidence of stricture. With more satisfactory anastomoses in recent years the need for subsequent dilatation has been infrequent.

RESULTS

That congenital atresia of the esophagus with or without tracheoesophageal fistula is a fatal condition unless an operation is done to provide some mechanism for nutrition is well known. The longest reported survival is thirty-seven days.[7] Mild degrees of stenosis without fistula, or small fistulas without other malformation of the esophagus are not necessarily fatal, however, some having been reported even into adult life. Of the 136 cases reported here, 35 were not operated upon, of which 20 were diagnosed during life. The longest survival among these was eighteen days, and the median age at death was 7 days. Of the 15 not diagnosed during life, 4 were stillborn, and 6 died during the first day of life. As has already been brought out, this group was small, often premature, and had a high incidence of associated severe malformations. The remaining 5 were discovered at autopsy, and must be considered missed diagnoses.

TABLE III

	CASES	SURVIVORS	SURVIVAL (PER CENT)
No operation			
Stillborn	4	0	
Died first day	6	0	
Diagnosed at autopsy	5	0	
Diagnosed but not operated upon	20	0	
Total	35	0	0
Operations performed			
Gastrostomy only	10	2	20
Gastrostomy and intraperitoneal ligation	1	0	0
Gastrostomy and exploratory thoracotomy	1	0	0
Gastrostomy and transpleural ligation	2	0	0
Gastrostomy and cervical stoma	2	0	0
Retropleural division and cervical stoma	13	5	38
Esophagogastrostomy	3	0	0
Esophageal anastomosis			
Transpleural	11	0	0
Retropleural	58	26	44
Total	101	33	33
GRAND TOTAL	136	33	24

The operations performed on the 101 patients for whom some procedure was done, are summarized in Table III. The diversity of method reflects the early transition period as well as later variations in response to unusual anatomic problems. It is clearly seen from this table that the 33 survivors fall into three groups. The first is the occasional patient with atresia but no fistula, who survives after gastrostomy only. Reconstruction of the esophagus can then be done at a later date. Only 2 such cases are included in this group. The second group is the 5 patients who survived the first successful method of dealing with tracheoesophageal fistula, consisting of retropleural closure

of the fistula, cervical esophagostomy and gastrostomy. Though the first patient to survive is now well at 14 years of age and swallowing normally, only one other of the 5 is similarly fortunate. The other 3 died, one at 3 months from aspiration pneumonia due to an unrecognized fistula between the trachea and upper segment, one at 2 years following acute gastric dilatation, and one at 3 years of tetralogy of Fallot. The third group of survivors are the 26 who were treated by retropleural anastomosis. This is obviously the most satisfactory method of dealing with the usual type 3b anomaly. With an over-all survival rate of 44 per cent, it is seen in Table II that this rate was improved to 66 per cent survivals in the last year reported. The most frequent cause of death in this group is respiratory failure in the first forty-eight hours after operation especially in small feeble babies, or those with other severe malformations. Breakdown of the anastomosis with secondary infection due to leakage, a common fatal complication in the earlier period, now occurs infrequently. When incomplete, recovery is possible but stricture often follows, requiring careful dilatation for periods up to a year or more. This complication may also follow anastomoses in which the lower segment is so small that formation of an adequate stoma is technically difficult. Such patients occasionally have difficulty due to lodging of solid food or foreign bodies in the esophagus, one of this series having been readmitted four times to remove pebbles, string, and food particles which caused obstruction. In no instance, however, has reoperation become necessary, and with growth a normal esophageal lumen and normal swallowing results.

SUMMARY

A brief history of the development of operative treatment for congenital anomalies of the esophagus at Columbia-Presbyterian Medical Center (Sloane and Babies Hospitals) in New York over the past one-half century is presented. This history parallels the experience in other centers and has resulted, beginning with the first survivor in 1942, in a salvage rate, in 1952, of 66 per cent. Factors influencing survival are seen to be the size and degree of prematurity of the infants; the association with other severe malformations; the awareness of doctors and nurses caring for newborn infants of the possibility of the condition and their alertness in recognizing the characteristic symptoms; the promptness with which patients are referred for surgery; the care in pre- and postoperative management; and the technical aspects of the operation itself. The first two factors are uncontrollable. The others leave room for improvement even in our own clinic. While occasional cases will present anomalies which require multiple-stage procedures before swallowing can be restored, in the majority of cases, successful end-to-end anastomosis of the esophagus is possible, with satisfactory restoration of normal swallowing.

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DISCUSSION

DR. ROBERT R. SHAW, Dallas, Texas.—This anomaly has been one that has occupied my interest from the time I started in practice in thoracic surgery. Like the experience of everyone else, at first it was a very dismal one, but later gave way to some optimism for expected recovery if a suitable infant was presented.

(Slide) This slide, which was prepared two years ago, shows our experience with this anomaly. Through the years up to 1948 there were only two survivals in 23 patients, but from 1949 on, the percentage of survivals became much better. During the years 1952-53, we had eight survivors out of 11 patients. The crux of success in the management of this anomaly is the anastomosis. We attempt to get an anastomosis in every patient and, in 56 cases of 61, an end-to-end anastomosis was accomplished. Admittedly, in many cases, the anastomosis was poor due to the fact that the segments were not of good length and there tended to be tension. Early leakage and late stricture formation are the complications resulting from poor anastomoses.

(Slide) This patient was interesting from the standpoint of multiple anomalies, in that the second anomaly other than the atresia of the esophagus, was obvious on the first film. This child had an atresia of the duodenum as shown by complete block at the second portion of the duodenum. However, this film was not available at the time of the first operation, since he was flown from a distant city to our city, and although five doctors came along, the x-rays were not brought with the patient. It soon became obvious that this second anomaly was present. It was also successfully repaired (by Dr. Warner Duckett of Dallas) on the twelfth day of life, and at the present time this child is a normal healthy boy of 6 years of age.

(Slide) This child is interesting because of the late period at which she was presented for surgery, and it illustrates the point that more reports of this sort should be in the pediatric literature. This child was 28 days old when she was brought to our clinic for repair of the atresia. The physician taking care of the child had advised the parents not to do anything about it even though the diagnosis had been made promptly after birth. He said if it were his own child he would do nothing about it. They had bought a burial plot and decided to let the child die. However, they did give the child a hypodermoclysis every day or so and kept it in some degree of hydration although it lost two of its six pounds birth weight in twenty-eight days. At the time of surgery an anomaly very easy to repair was found and, because I felt that the anastomosis was adequate and the child's situation was somewhat precarious, I started the baby on mouth feedings the day following surgery. You can see by this slide that in eight days it was very difficult to demonstrate the point of anastomosis. We were never able to fill the baby up, she was so hungry. Sometimes even with late arrival of these children it is possible to salvage them.

DR. CAMERON HAIGHT, Ann Arbor, Mich.—The subject has been covered so thoroughly that I have very little to add, but I particularly wish to commend the authors on the very excellent study which they have done. There are so many variable problems in these infants that it is difficult to compare statistics and I shall not do so. The noncontrollable factors which have been emphasized are of great importance and contribute

importantly to the results that can be obtained. We have been seeing a number of these infants with associated congenital heart disease and other anomalies, some of which in themselves are not compatible with life. We have come to the opinion that associated congenital heart disease should be treated by early operation if feasible for the reason that 4 of our earlier patients died as a result of their cardiac lesions. Although we have operated upon 4 patients with postoperative atresias for cardiac lesions, only one so far has been successful.

Another noncontrollable factor, at least to the surgeon, is the amount of pneumonitis which may have been precipitated by the preadmission use of contrast material and its entry into the lung. Although most of our infants have had Lipiodol contrast studies before admission, we believe that Urokon is a preferable roentgenologic agent if contrast material is to be used, but I have doubt as to the advisability of using any contrast material at all.

A controllable factor is the antibiotic coverage which is employed. For some years we have felt that the use of penicillin, streptomycin, and polymyxin B provided adequate antibiotic coverage; we find, however, that this is not enough and recently we have used a wide spectrum antibiotic in addition. With an all-inclusive type of antibiotic coverage, it is hoped that complications from controllable factors, such as pneumonitis and leakage of the anastomosis, can be avoided and that the recovery rate will thereby be improved.

DR. RALPH BERG, JR., Spokane, Wash.—I enjoyed this presentation very much also, and I have a patient that may be of interest.

(Slide) This child was operated on at about 18 hours of age. There was a proximal pouch end at this area. There was no fistula and no distal esophagus except for a small nubbin about 2 mm. above the diaphragm.

(Slide) This shows the repair accomplished by a transpleural approach with primary esophagogastrostomy.

(Slide) This is the child about one year postoperatively. The child is now three years postoperative and has had a stricture dilated five times.

Since this seemed unusual, after perusing the literature I present it at this time and would like to know if the authors had any similar patients in their series. I could not tell from the presentation.

DR. OSLER ABBOTT, Emory University, Ga.—I should also like to compliment this paper. I think certainly the name of Dr. Ladd should be mentioned whenever a discussion of this subject is brought up.

There are two things I should like to mention briefly. One is with regard to the use of Lipiodol, as mentioned by Dr. Haight. We have been interested in the bacterial content of the upper stump; it has a high content in some instances of anaerobic streptococci and we think the potential of the material in the upper stump has not been adequately emphasized. We recently had an episode of a fatal lipoid pneumonia due to overflow spillage of Lipiodol from the upper stump. Lipiodol was overzealously and overgenerously given in an x-ray department elsewhere. We have been struck recently with the importance of aspirating the upper stump with a catheter and then distending the upper stump with air, so that we get our contrast without soilage of the lung and without tendency to aspiration. We would like to mention the importance of the so-called H-type of fistula without atresia, which we have seen on three occasions, recognition of which can be very much delayed, and which does give a very happy result when found. One of our 3 had multiple associated anomalies; the other 2, one of which was recognized at 4 days of age, were successful.

Finally, I would like to mention that we are having trouble with reconstruction in the exteriorized patients who are now in their sixth, seventh, and eighth years, and we wish, in retrospect, that when we had brought the esophagus out into the neck, we had

brought it out on the left side, which is the more normal anatomic deviation of the upper esophagus and does allow a better anastomosis to the stomach or other tissue brought up under the sternum.

DR. WILLIS J. POTTS, Chicago, Ill.—This fascinating subject is worthy of much discussion. There is probably no operation which is packed with so many disappointments and heartaches as those on this particular group.

During the past ten years we have operated on approximately 125 patients with tracheoesophageal fistula plus the usual atresia of the upper end. It is our policy to operate on every child regardless of its condition—provided, of course, that it is still breathing, because there is no chance for the child without surgery. During the first five years, our mortality varied from 40 to 70 per cent. Then we made a number of radical changes. Now the mortality has dropped considerably: to 40 per cent in 1953, to 20 per cent in 1954, to 11 per cent in 1955. A few tough cases probably will alter our good fortune. However, we believe that some of the things that account for this improvement are: (1) intratracheal anesthesia, which we used to think was harmful for infants; (2) transpleural approach, which is much faster; using the extrapleural approach remains so about one-half the time, the rest of the time there is just a touch of the intrapleural; (3) an anastomosis, end-to-end, with two layers of No. 6-0 silk suture; (4) in the postoperative period the residents and nurses are constantly alerted to the dangers of aspiration and they all know how to aspirate these infants and keep the trachea clear; (5) the feeding of these children. It took a long time to convince the nurses that they had to feed these children with a medicine dropper. If, during the early postoperative period, one feeds these children with a nipple, the hungry child will eat too fast. The upper end of the esophagus fills because of the usual minimal or moderate stricture at the site of anastomosis. The child regurgitates and before anything can be done, he has drowned in his own formula. It is difficult to convince the nurses and one must be after them constantly. With a medicine dropper they can give only one cubic centimeter at a time and the tragedy of drowning and aspirating formula into the lungs will be avoided.

DR. RICHARD KING, Atlanta, Ga.—There is one complication I would like to mention, that is, the redevelopment of a fistula after the initial procedure.

This occurred in a case of mine in September, 1955. The postoperative course was uneventful for approximately three weeks. The baby at this time began to have respiratory difficulty at the time of feedings, with paroxysms of coughing and cyanosis. An esophagram was done and a fistula was demonstrated between the esophagus and trachea at the site of the closure of the trachea and the anastomosis of the esophagus. A right transpleural thoracotomy was done again, and the fistula between the trachea and the esophagus was located and taken down. The openings in the trachea and the esophagus were then closed with interrupted silk sutures. To prevent redevelopment of the fistula, a pleural graft was sutured between the esophagus and the trachea. I feel that the use of a pleural graft is a very important part of the procedure and that it should be used in all cases at the initial procedure.

Drs. Shaw and Paulson in their excellent article on the subject last year mentioned the use of mediastinal fascia between the trachea and esophagus to prevent development of a fistula.

DR. GEORGE H. HUMPHREYS, New York, N. Y. (Closing).—I wish to thank all the discussants. We could go on discussing this subject for a long time because there are so many bad results and so many different ways of getting them. At the outset, I should like to assure you that the paper gives due emphasis to the pioneers in this field. One thing that interested us was the fact that there were people working in various centers on the same subject at about the same time. I believe Dr. Lanman had worked with Dr. Ladd on these babies for a number of years at Children's Hospital in Boston, and that Dr. Ladd was disappointed to find that his first survivor was operated on just

one day after Dr. Logan Leven's survivor, because neither knew of the work of the other. Our first survivor was operated on several months later by a similar technique. We also did not know at that time of the successful cases of either Dr. Leven or Dr. Ladd.

Dr. Shaw and Dr. Haight both were pioneers in the field, and to Dr. Haight goes the credit of demonstrating that direct anastomosis is the obvious and best procedure. We had given it up after several failures, apparently prematurely, because we now know how to do it as Dr. Haight has shown us. The obstruction that Dr. Shaw showed is very interesting. We also had 2 cases of obstruction, one at the duodenum similar to his, and one hypertrophic pyloric stenosis. These must be watched for, especially if feedings do not go well.

The antibiotic coverage which Dr. Haight emphasized is extremely important, and certainly the difficulties with the bacteriology and the contrast medium in the stump as described by Dr. Abbott are a common experience with all of us, and must be looked for. I think contrast material is a mistake. It is not necessary, the stump can be demonstrated, the lesion can be demonstrated by a double catheter or, as he suggests, by air, and it is far better not to use any contrast medium. Unfortunately, however, we usually get the patients with contrast medium already in them.

Dr. Potts has brought out the factors which implement survival, and his survival rate certainly depends on all of them. I would emphasize particularly, as he did, the postoperative care both in feeding and in aspirating these patients. Both the house staff and the nursing staff should be specially instructed, there should be special people who know how to handle these babies, otherwise the mortality is bound to be higher. I take issue with him only on the intrapleural approach, but this is a small factor and probably not important.

We did not encounter recurrence of a fistula. I think perhaps the method of closure of the membranous portion of the trachea is a large factor in this. We were lucky in the first few cases in which we ligated, and now we close it very carefully with interrupted fine silk and have had no difficulty on that score.

TOREK ESOPHAGECTOMY

The Case Against Segmental Resection for Esophageal Cancer

William L. Watson, M.D., John T. Goodner, M.D. (by invitation), Theodore P. Miller, M.D. (by invitation), and George T. Pack, M.D. (by invitation)
New York, N. Y.

AN INTIMATE knowledge of the anatomy of the esophagus is helpful in understanding the peculiar dangers and difficulties encountered in the treatment of cancer of this organ. One recalls that the esophagus is a thin-walled flexible muscular and mucosal tube about 25 cm. in length. The esophagus differs from the other portions of the intestinal tract in that it lacks an outer, serosal covering and this is a distinct surgical disadvantage.[5] The esophagus has a scanty blood supply, but a rich network of lymphatic vessels in its submucosal and muscular coats which provide a ready submucous pathway for the lymphatic dissemination of cancer.

From the surgical point of view, it is obvious that the thoracic esophagus is deeply situated and intimately surrounded by important and vital structures which are often invaded early in the natural course of esophageal cancer. The esophagus is insensible to pain stimuli and when backache, substernal discomfort or pain do exist it is almost certain that disease has extended through the esophageal wall into the mediastinal structures. Since pain is a late symptom, it follows that cancer of the esophagus when first diagnosed is apt to be an advanced disease.

From the anatomic viewpoint, the esophagus provides a fertile field for the silent development and spread of intrinsic cancer and at the same time it poses serious and sometimes insurmountable obstacles in adequate surgical management.

LYMPHATIC SPREAD OF ESOPHAGEAL CANCER

Cancer of the cervical portion of the esophagus spreads early and with great regularity to the anterior, superior mediastinal as well as the lower deep jugular and prescalene lymph nodes. If the malignant growth is located in the lower third of the esophagus, the dissemination is usually by way of the extrinsic lymphatics to the periesophageal and perigastric lymph nodes. Mucosal and submucosal extension downward into the cardia of the stomach often causes some question as to whether the primary cancer arose in the esophagus or in the stomach.

Read at the Thirty-sixth Annual Meeting of The American Association for Thoracic Surgery at Miami Beach, Fla., May 7 to 9, 1956.

The upper third of the thoracic esophagus is apt to develop large, ulcerating, badly infected cancers which metastasize readily by way of the rich submucosal lymph vessels into the adjacent mediastinal lymph nodes (Fig. 1). It

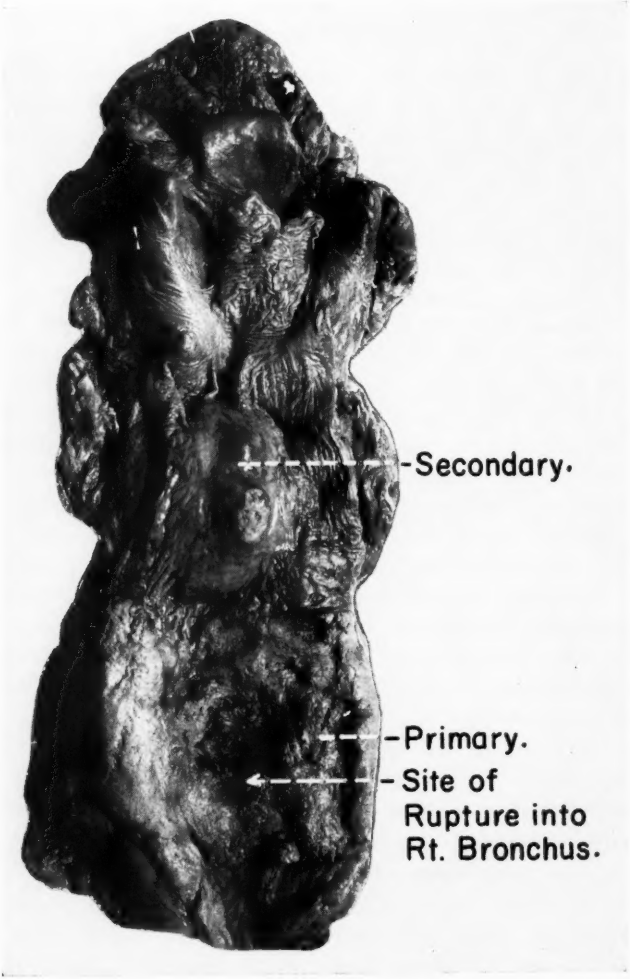

Fig. 1.—The gross specimen shows a large primary carcinoma of the esophagus perforating into the right bronchus causing death by asphyxia. A large secondary growth 5 cm. in diameter is seen several centimeters above the primary lesion. Microscopic section showed the lesion to be an epidermoid carcinoma, grade III.

is important to note that these same intramural lymphatic vessels also distribute the neoplastic cells in a longitudinal direction often to a considerable distance above or below the visible or palpable limits of the primary cancer.

Viable tumor emboli may block a lymphatic branch and give rise to a secondary deposit which presents as a submucosal outcropping (often under an intact mucosa) sometimes as much as 8 cm. distant from the primary cancer.

The above data were first noted during the study of a number of gross specimens of esophagus cancer by serial microscopic examinations. Prior to this work of 1933, it was not uncommon to encounter, in the literature, case reports of multiple esophageal cancer. It is now our opinion that in most instances these were examples of submucosal cancer metastases. Simultaneous, multiple esophageal cancers probably are most uncommon.

Doctors, in general, agree that an adequate surgical operation for cancer requires a wide resection of the primary growth in continuity with the regional lymphatic vessels and lymph nodes. In the case of cancer of the esophagus, the surgeon's attention has been focused on the lateral spread of disease and its extension into structures and little attention has been paid to the longitudinal dissemination of the disease. Perhaps as a result of the known poor prognosis for malignant lesions of the upper two thirds of the esophagus, surgeons have come to regard resections in this area as primarily palliative procedures requiring only a local resection of the tumor with immediate reconstruction.

An early review of our cases of esophageal resection indicated a higher incidence of inadequate longitudinal excision than we had anticipated.[3] Seventy-nine cases were analyzed and 45 per cent of the patients with esophageal cancer who were subjected to segmental resection had an inadequate longitudinal removal of their disease. Surgical failure was established in the following criteria: (1) Microscopic evidence of cancer at the margins of the resected surgical specimen, (2) subsequent microscopic evidence of recurrent tumor by biopsy obtained at the line of anastomosis, or (3) microscopic proof of tumor at the line of anastomosis in the autopsy specimen. Pathologists are prone to take longitudinal specimens at the line of esophageal transection for immediate frozen section diagnosis at the time of operation and it seems clear that transverse sections are required if one is to discover submucosal lymphatic cancer at the site of resection.

In order to cut down the local recurrence rate and possibly increase the cure rate, it was obvious that a longer portion of the esophagus needed to be removed and it was decided to do a series of Torek esophagectomies. Forty-eight patients had this type of excisional surgery. The original Torek esophagectomy, successfully performed in 1913, left the patient with a messy anterior chest wall esophagostoma and a troublesome gastrostomy feeding problem. Both these features of the operation are undesirable.

The esophagectomy we favor is similar to that of the Torek operation only in that it is done for cancer and, as far as possible, all the esophagus with its lymphatics is removed. The operation differs from Torek's procedure in that our approach is through the right chest and an immediate or staged esophagoplasty is carried out. Only 31 of our 48 patients who had total esophagectomy for cancer of the upper two thirds of the thoracic esophagus were suitable for esophagoplasty.

Six different methods of esophagoplasty have been given a trial. The first attempts employed rubber and plastic tube contrivances. After trying a few of these, the results were unsatisfactory and they were given up as hopeless (Figs. 2 *A* and *B*). Next we tried cutaneous, anterothoracic esophagoplasty in 6 cases and ran into the usual complications of gastric regurgitation, ulceration, stenosis, and prolonged morbidity (Fig. 3). In 2 cases an anterothoracic jejuno-esophagostomy (Fig. 4) was carried out and in 4 cases a retrosternal jejuno-esophagostomy was done. One of these patients is alive and free of disease more than five years after surgery. We also had some success with gastroesophageal anastomosis in the neck; this type of esophagoplasty was carried out in 10 cases.

In the last seven attempts at total esophagoplasty, we have employed retrosternal right colon transplants. In reporting this small group, it must be kept in mind that each patient had cancer located in the upper two thirds of his esophagus and in each instance the lesion was resected through a right thoracotomy incision by a procedure which in some respects is similar to the one devised and successfully carried out by Dr. Franz Torek in 1913. The use of right colon for total esophagoplasty is not a new idea. It was first reported in 1911 by Kelling[1] and, in 1934, Ochsner[2] collected 20 case reports from the literature. The majority of these were from European clinics and the surgeons brought the colon up to the neck through a subcutaneous tunnel. Dr. Charles D. Sherman[4] has called attention to the value of this type of esophagoplasty and has recommended the use of a retrosternal tunnel for the transplanted colon.

The procedure which we follow for cancer of the upper two thirds of the esophagus consists of two stages. First, a Torek type total esophagectomy through a right posterolateral thoracotomy and at a second stage, two weeks later, a right colon substernal esophagoplasty.

INTRATHORACIC RIGHT COLON ESOPHAGOPLASTY

In addition to the usual large bowel preparation for surgery, it is advisable to have a routine barium enema to determine the approximate length of the right colon and rule out any pathologic condition of that portion of the bowel.

(Fig. 5) At operation, after mobilization of the right colon, the right colic artery is temporarily occluded for fifteen minutes during which time the appendix is removed and the stump inverted (Fig. 6). If the blood supply to the cecum is adequate and arterial pulsations are visible then the occluded blood supply is divided. The transverse colon is divided just to the left of the mid-line. The terminal ileum is then divided and its distal end turned in after which bowel continuity is re-established by end-to-end ileotransverse colostomy.

(Fig. 7) A retrosternal tunnel is developed and the colon is brought through it taking care not to twist, kink, or otherwise compromise its blood supply. The cecum is anastomosed to the distal cervical esophagus and the final step is the anastomosis of the lower end of the colon transplant into the

Fig. 2.—*A*, Front view. Torek esophagectomy performed July 16, 1941, for cancer. Temporary rubber and glass apparatus permits the patient to take fluids and swallow his saliva.

Fig. 2.—*B*, Oblique view. Torek esophagectomy performed July 16, 1941, for cancer. Temporary rubber and glass apparatus permits the patient to take fluids and swallow his saliva.

Fig. 3.—Torek esophagectomy performed April 8, 1954. The gross specimen revealed a submucosal metastasis 6 cm. above the primary growth. A cutaneous anterothoracic reconstruction was made on May 6, 1954.

Fig. 4.—Torek esophagectomy performed on Oct. 3, 1949, for cancer. Anterior thoracic jejunoesophagostomy, May 18, 1950. Patient is alive and well six years later.

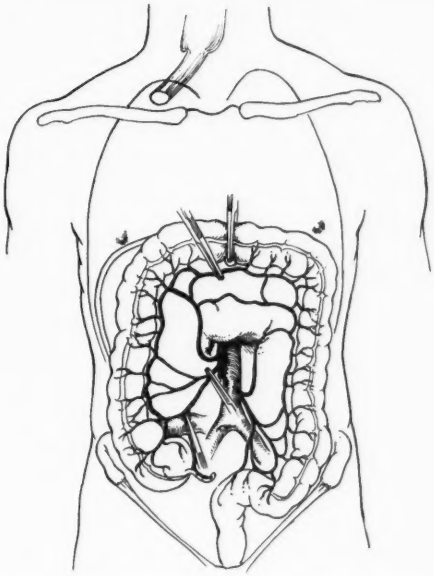

Fig. 5.—The right colon has been mobilized and arterial clamps applied to the right colic artery and all other blood supply except that through the middle colic artery.

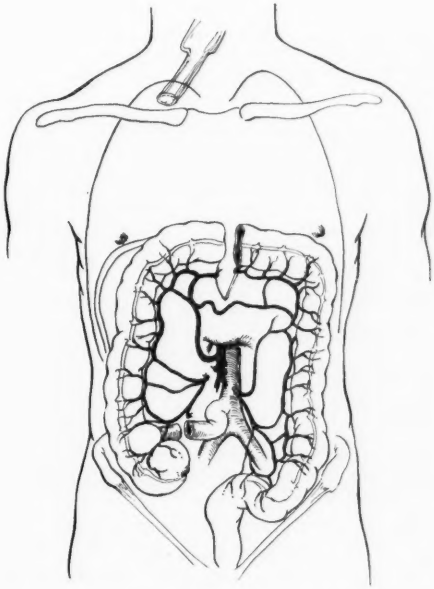

Fig. 6.—The transverse colon is divided just to the left of the mid-line. The terminal ileum is divided and the end turned in.

anterior wall of the stomach. After the wounds are closed a chest roentgenogram is taken in order to detect any evidence of pneumothorax which would require correction.

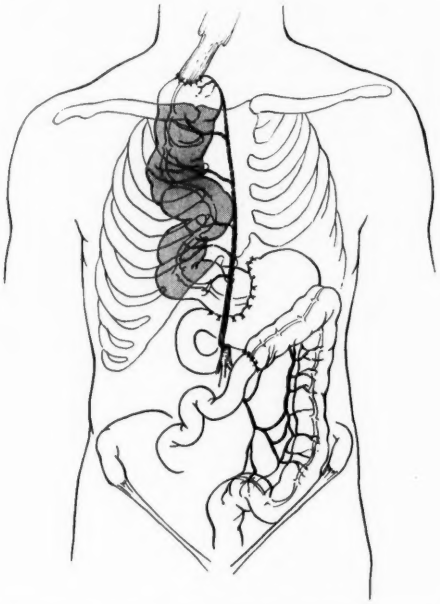

Fig. 7.—Bowel continuity is re-established by end-to-end ileotransverse colostomy. The right colon segment is brought up through a substernal tunnel into the neck where it is joined to the cervical esophagus. The lower end of the colon transplant is anastomosed to the anterior wall of the stomach.

CASE REPORT

F. A., a 56-year-old white man, pharmacist, whose present illness began three months prior to hospital admission with slight "heart burn" followed soon afterward by dysphagia. During the following two months, the dysphagia gradually increased in severity until solid food could not be taken and even liquid food caused considerable difficulty and some discomfort.

On the first visit, his physician made radiographic studies and a clinical diagnosis was established and the patient advised to come to the United States for surgical treatment. During the present illness, the patient lost about 10 pounds.

X-ray studies (Fig. 8), including fluoroscopic examination of the esophagus, and esophagrams were reported as showing carcinoma of the mid-portion of the esophagus, measuring 3 cm. in length and showing partial obstruction to the barium flow. Chest films were normal.

Esophagoscopy and bronchoscopy were carried out July 18, 1955, and a biopsy from the esophagus, at 33.5 cm. from the upper incisor teeth, was reported as showing epidermoid carcinoma. A normal tracheobronchial tree was encountered on bronchoscopy. The medical and laboratory evaluations of this patient for surgery were reported as good.

On July 22, 1955, a Torek type of esophagectomy was carried out without incident through a right posterolateral thoracotomy incision. The patient made a most satisfactory postoperative adjustment and was fed adequately by gastrostomy tube (Fig. 9).

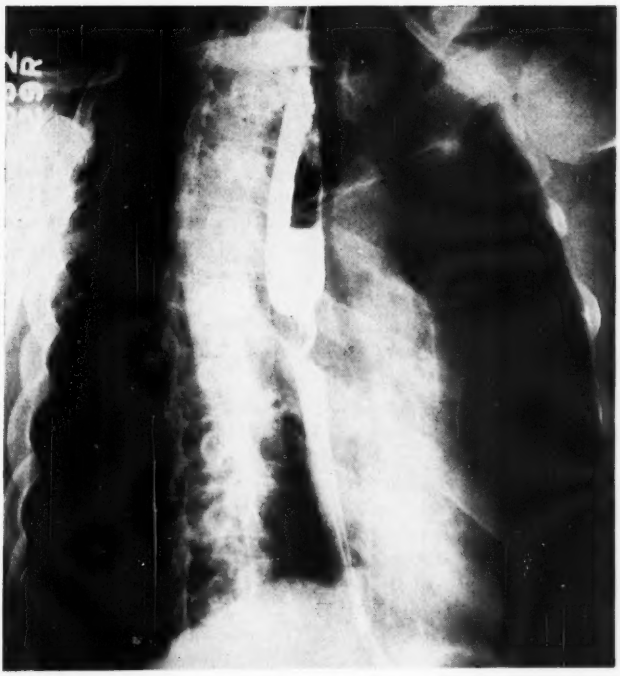

Fig. 8.—Esophagram made July 15, 1955, showing cancer in the middle third of the thoracic esophagus.

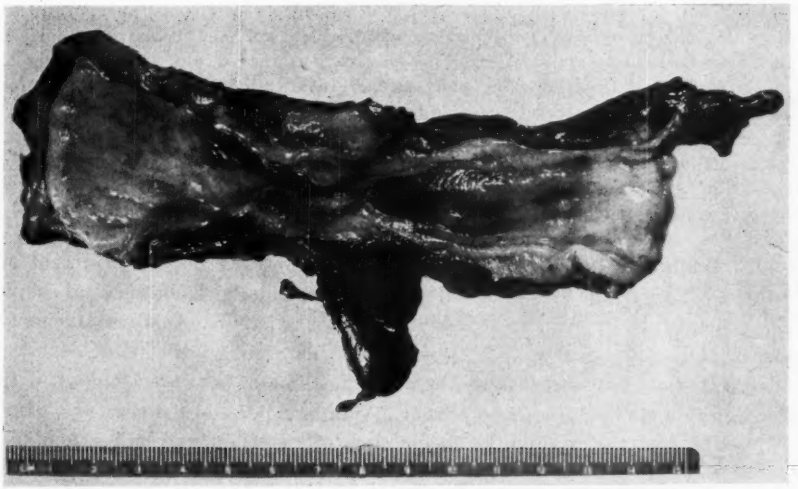

Fig. 9.—The surgical gross specimen consists of a 16 cm. segment of esophagus. Attached to the middle of the specimen were two soft gray-pigmented lymph nodes. The largest was 3 cm. in its greatest diameter. These were microscopically negative for tumor. The opened esophagus revealed an ulcerated tumor mass located in the middle third of the specimen and measured 2.5 cm. in its longitudinal axis. The upper margin of the tumor was 6.5 cm. from the margin of excision and the lower margin of tumor was 7 cm. from the lower margin of excision. The histologic diagnosis was epidermoid carcinoma of esophagus, grade II. Attached nodes were negative.

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Sixteen days after first stage (Torek esophagectomy), a second stage was carried out at which time a total esophagoplasty was accomplished using the right colon in the form of a retrosternal transplant, anatomosing the ileum with the cervical esophagus and the transverse colon to the stomach. An end-to-end anastomosis was established between the terminal ileum and the transverse colon.

The patient's postoperative course was somewhat complicated due to difficulty with the gastrostomy feedings and he developed a small cervical fistula, but otherwise the convalescence was not particularly unusual. However, on the nineteenth day following the second-stage operation (Aug. 28, 1955), the patient complained of some abdominal cramplike pain and a firm pulsating mass was noted in the right neck at the level of the anastomosis. The wound was opened at its lateral margin and a slight amount of sanguineous purulent material was obtained and it was planned to open the mass, which was thought to be an abscess, in the operating room the following morning. About 6:55 A.M., the patient became excited, dyspneic, anxious, pale, broke out in a cold clammy perspiration and went into severe shock, bleeding from the mouth, from the cervical wound, and also from the gastrostomy.

He died forty minutes later, obviously of a massive hemorrhage. Permission for an autopsy was obtained. The final anatomic diagnoses were as follows: (1) Epidermoid carcinoma of esophagus, postesophagectomy status. (Surgical diagnosis established on basis of biopsy and gross specimen.) (2) Recurrent epidermoid carcinoma, anastomotic site, metastatic to right cervical lymph nodes. (3) Peri-anastomotic abscess communicating with anastomosis and carotid artery with massive hemorrhage into cervical tissues and gastrointestinal tract. (4) Bilateral pleuritis, marked interstitial pulmonary fibrosis, focal atelectasis, infarction, bronchopneumonia, and emphysema. (5) Narrowing of ileocolonic anastomosis with dilatation of the proximal bowel. (6) Minimal acute and chronic pyelonephritis. (7) Extramedullary hematopoiesis. (8) Therapy: Esophagectomy, reconstruction of esophagus with terminal ileum. Transfusions, antibiotics. The colon transplant was viable throughout its length.

The important point in this case is the autopsy finding of recurrent epidermoid cancer of the site of anastomosis of the colon with the cervical esophagus. The surgical specimen revealed a minimal distance of 6.5 cm. of normal mucosa and esophageal wall between the upper limit of the palpable cancer and the line of operative transection. At the time of surgery a biopsy of this area was reported as free from cancer. Within a period of five weeks, cancer had recurred at this seemingly normal line of resection and had extended to a point where it had produced a fistula and an abscess and destroyed a portion of the common carotid artery in addition to producing cervical lymph node metastases. It is believed that this is a clear-cut example of the tendency for carcinomas of the mid-thoracic esophagus to extend considerable distances in a longitudinal fashion by way of the submucosal lymphatics.

SUMMARY

Longitudinal spread of esophageal cancer by way of the submucosal lymphatics is a common cause of recurrence at the site of esophageal transection.

Segmental resection for esophageal cancer was an inadequate operation in 45 per cent of 79 cases studied.

Total esophagectomy permits a more adequate removal of potentially involved esophagus.

Esophagoplasty using the right colon has been a satisfactory method of reconstruction in 7 cases.

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Discussion

MR. PHILIP ALLISON, Oxford, England.—I must first of all excuse myself to this extent. During the first part of this paper, I was carrying out something outside this room at the President's direction, so I find it difficult to discuss a paper which I have not heard in full.

I have become rather defeatist about carcinoma of the middle third of the esophagus. I agree with what I heard the speaker say about the longitudinal spread of the disease in the esophageal wall and I imagine that he probably discussed earlier the outward spread into the mediastinum. If we accept the general principle of resection of carcinoma with a wide margin of normal tissue around it, then a proper operation for carcinoma of the upper or middle third of the esophagus is impossible. The presence of nonresectable vital structures in immediate contact with the esophageal wall precludes the resection of a margin of normal tissue. I have not myself used reconstruction by the colon and I was much interested to hear of this work.

DR. RICHARD H. SWEET, Boston, Mass.—I hoped to hear from some of the other members on this subject, but inasmuch as you have been good enough to ask me to comment, I would like to say that although I certainly feel that Dr. Watson has brought out a good point with regard to the longitudinal spread to the lymphatics, I fail to see that he has given sufficient emphasis to the involvement of the lymph nodes. In the days before I was doing primary anastomosis and was still doing the Torek operation, more, perhaps, according to the original Torek technique, I made it a practice to explore the upper abdomen through the chest and was interested to observe that in at least two thirds of all the cases the lymph nodes there were involved. Because I felt that the limitations of the procedure were such that I could not remove those nodes adequately, I abandoned the operation in those patients. Since it has been possible to enlarge the scope of the procedure, however, I have felt and still feel that the Torek operation has no place in the treatment of carcinoma of the esophagus. I believe very definitely that one should make every effort to remove all the lymph nodes which are involved in the downward lymphatic spread of the metastases. This should include the pericardial group and also the nodes in the

region of the left gastric vessels. It appears to me, at least from one of the specimens demonstrated today, that those nodes perhaps are not being excised in the operation advocated by Dr. Watson.

One other comment about the longitudinal spread. It almost seems that when the pathologist reports that cancer cells are found at the point of transection of the esophagus, the prognosis is bound to be very good indeed. Recently I had a patient walk into my office who said to me, "You know that this is the thirteenth year since you did the operation." I looked back into the record and, sure enough, the pathologist reported that I had cut through tumor cells in the lymphatic channels.

DR. WILLIAM E. NEVILLE, Cleveland, Ohio.—I want to compliment Dr. Watson on his excellent presentation; we certainly agree with everything he has said. Dr. Clowes and I became interested about two years ago in the use of the colon to replace the esophagus and to date have operated on 14 cases, with four deaths in the immediate postoperative period. We feel, at the present time at least, that the colon offers several distinct advantages; (1) it has an excellent blood supply; (2) it is of sufficient length to reach the neck in case of high resection; and (3) it may be more resistant to peptic ulceration than the jejunum or the stomach.

(slide) This is one of our earlier cases. You can see the proximal suture at the level of the aortic arch. The distal end of the transverse colon is anastomosed to the stomach.

(slide) This is our highest resection for carcinoma to date. The lesion was delivered into the neck and anastomosis performed above the clavicle as demonstrated on the slide on the right.

(slide) This is probably our most intriguing case. This child had a tracheoesophageal fistula which was impossible to anastomose. For this reason, an esophagostomy was performed with a feeding gastrostomy. When the patient was one year of age, we reconstructed the esophagus with the transverse colon. To date he has gained weight and has an excellent nutritional status.

DR. JOHN H. GARLOCK, New York.—In the interest of historical accuracy it is important to remember what the original Torek operation consisted of. It really was not a subtotal esophagectomy at all. In the first place, no attempt was made to find out what was going on below the diaphragm with respect to retrograde lymph node spread and, in the second place, a considerable portion of the esphagus was always left above and brought out to form the upper esophagostomy stoma at a point approximately opposite the left second rib. This was certainly not a subtotal removal.

It is now almost twenty-one years since we started working on this problem and I must say that we have learned a great deal about the life history of this disease. We utilized the Torek operation in the first 16 cases subjected to esophagectomy and it did not take us long to find out that recurrences could occur at the site of the upper esophageal stoma. In the early days, we did not appreciate the significance of this but it soon became evident that this local recurrence was due to submucosal spread proximally. I believe that it is just as important to stress the fact that retrograde spread may occur below the diaghragm even with carcinomas as high as the arch of the aorta. This spread usually involves the nodes along the course of the left gastric artery and in the pericardial area. Any operation which does not include the removal of this lymphatic region below the diaghragm cannot be considered an adequate extirpational cancer procedure. I agree fully with Dr. Watson that it is important to have a wide resection proximal to the tumor. We have been stressing this point for some years now and have gone so far as to advise subtotal esophagectomy for carcinomas of the distal third in order to get beyond the upper limits of the submucosal spread.

It is always interesting to hear about the revival of operations in which other organs are utilized to restore gastrointestinal continuity. Last year, I visited that dynamic Japanese surgeon, Nakayama, and I had many discussions with him and saw him operate a number of times. He has had a high incidence of breakdown due to interference of blood

supply of the upper end of the stomach when he utilized an intrathoracic anastomosis. In practically every case now he is placing the stomach subcutaneously which is again a rejuvenation of an old operation. He effects an almost subtotal esophagectomy, brings the stomach subcutaneously as far as the neck and makes his anastomosis with the esophageal stump beneath the skin. He claims that if he gets a breakdown, it is much better to have it under the skin than in the chest and I am sure that everyone here will agree with him. It might surprise you to learn that he accomplishes this operation in the brief span of one hour and fifteen minutes.

DR. WILLIAM L. WATSON, New York, N. Y. (Closing).—I should like to thank those who were kind enough to discuss our report. We share Mr. Allison's pessimism regarding esophageal cancer in general, and, in going over the results in our 1,700 cases, we were unable to find a single five-year survival in the group of cancers located between the thoracic inlet and the aortic arch; these are the cases discussed in this report.

Dr. Sweet brings out the point that he always explores the upper abdomen first, but of course lesions of the upper one-third of the esophagus do not routinely metastasize to the upper abdominal lymph nodes, and if such metastatic lymph nodes are present they do not necessarily contraindicate excisional palliative surgery. At our second-stage procedure, the upper abdomen is thoroughly explored and regional metastatic lymph nodes are removed.

It was good of Dr. Garlock to point out the dissimilarity between our operation and the ones so ably done by Dr. Franz Torek. He is correct, and yet I believe we both desire to give Torek the credit for his pioneer work; certainly the operation of esophagectomy first recommended by Dr. Torek could not be called a segmental resection. It was more than that—in other words it was a subtotal esophagectomy.

CARDIAC SURGERY WITH HYPOTHERMIA AND ACETYLCHOLINE ARREST

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TOTAL body hypothermia has been shown to protect vital organs from prolonged periods of oxygen deprivation.[1-3] The suppression of metabolic activity that is the basis for this and the sensitive temperature modalities of cellular enzymatic reactions suggest real hazard associated with the use of temperatures far from body normals. Holding the period of circulatory stasis to a minimum has prevented the appearance of cerebral, renal, and hepatic complications; however, there has been trouble with the heart itself, clinically with abnormal hearts and experimentally with normal hearts. The major complication, and of a consequence the major deterrent to the use of clinical hypothermia, has been the occurrence of ventricular fibrillation.[4, 5] Fibrillation has appeared during cooling and warming; therefore, the hypothermia per se has been considered the major factor causing ventricular fibrillation. Undoubtedly there is an increased sensitivity to fibrillation from the hypothermia. Attempts to obtain precise physiologic data to explain this have shown refractory period variations, retardation of depolarization and repolarization in pacemaker tissue, etc.,[6] but there has been no finding to settle this issue. Hypothermia (to 20° C.) alone does not lead to cardiac failure[7] and oxygenation of the myocardium is more than adequate.[8]

Unfortunately, it has been impossible to have all data associated with controlled ionic and acid-base relationships. In fact, many experiments are such that one cannot even guess the general trend—acidosis, alkalosis, or normality. Our experience is apropos. The generally recommended method of hyperventilation to a state of alkalosis[2, 4] has been associated with considerable presurgery ventricular fibrillation in our experiments, and this hazard increased at the lower temperatures.

Maintenance of a near normal acid-base balance with self-ventilation during cooling and minimal respiratory assistance when the chest was open has altered the picture.[9] Since adopting this method the only animal (of 90) that has had ventricular fibrillation prior to cardiac manipulation and surgery has been one with a heart full of worms. Niazi and Lewis have had excellent results with the use of added CO_2 which helps to maintain normal

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This study was supported by the E. F. Andrews Fund for Thoracic Surgery and by grants from the Simms and Oscar Mayer Foundations for Medical Research.

Read at the Thirty-sixth Annual Meeting of The American Association for Thoracic Surgery at Miami Beach, Fla., May 7 to 9, 1956.

serum pH.[10, 11] Fisher and co-workers[12] have used simple self-ventilation in their studies and have had no ventricular fibrillation until after six and one-half hours of 22° C. hypothermia.

When circulatory stasis has been added, it is our impression that this is the major factor relative to the production of ventricular fibrillation, to the cardiac damage which produces the failing heart, to the rhythm disturbances during warming, and to some postoperative deaths. When the surgical procedure produces a valvular abnormality or coronary insufficiency, a more lethal factor may be introduced.

The heart is protected from loss of coronary circulation by the hypothermia. At normal temperatures the excluded heart will deteriorate in one to three minutes and will rarely tolerate more than five minutes *while still contracting.* The hyperthermic heart (42° C.) will go into lethal standstill within a few seconds after inflow occlusion.

From this point of view, there are three approaches to gain further protection for the heart with hypothermia: (1) stopping or profoundly inhibiting cardiac activity during the period of circulatory stasis to diminish useless metabolic activity, (2) giving oxygen to the myocardium during the cardiotomy time, and (3) decreasing cardiac sensitivity with antifibrillatory drugs.

Combinations are also important, and it is probable that a part of the effect of many antifibrillatory drugs is in their concomitant slowing of cardiac rate (and therefore work).

METHOD

Preparations and procedures were essentially the same for experimental animals and patients. Morphine sulfate was the only medication given prior to surgery. Atropine-like compounds were avoided because they block the effect of the acetylcholine. Ether-oxygen anesthesia was used in amounts just sufficient to produce sleep and prevent shivering. Self-ventilation was allowed to the time of opening the chest, although an occasional animal required episodic assistance to respiration. This maintains a relatively normal acid-base relationship. When the thoracotomy was performed and assisted respiration needed, only 3 cycles were made in each minute (with the temperature between 20° to 26° C.). Inspiratory and expiratory carbon dioxide volume percentages were constantly monitored (at oral level) with a recording Liston-Becker CO_2 meter.*[9] This was especially helpful in judging the character of assisted respiration. After initial problems with excessive and accumulated tracheobronchial secretions and persistent pneumothorax, presumably due to the fact that no atropine was used, repeated intratracheal aspirations were performed during cooling and warming. Such difficulties have not been encountered in the human patients. Cooling and warming were accomplished with a commercial circulating fluid blanket with pump and temperature modifying unit (Therm-O-Rite). A direct reading galvanometer with attached rectal thermocouple was used to monitor temperature. Repeated checking was done with a mercury thermometer. With this

*Modified for constant recording and instantaneous calibration by Dr. E. T. Mörch.

slow cooling, the intrathoracic temperatures were quite close to the rectal ones. In clinical cases, excessive cooling of feet and pressure areas was avoided by repeatedly checking temperatures of the skin at these sites and by insulating when low temperatures were obtained. This has been extremely important with infants as peripheral temperatures will fall to 10° C. long before the surgical temperature is attained. Procedures on the patients were performed at 22° to 26° C., in the animals at 20° to 28° C. Limb Lead II electrocardiogram has been used as a monitor throughout the procedures. A plastic catheter cannula was inserted into the femoral artery of the cooled animals for pressure recording. Arterial pressure and electrocardiogram were recorded continuously on a Grass ink-writing electromanometer, a P23D Statham strain gauge has been used as the pressure transducer. Appropriate right, left, or bilateral thoracotomy was performed as needed for the operation. Cardiac exclusion was accomplished by occluding the azygos vein and both venae cavae, halting respiration, allowing the heart to empty, and cross clamping the aorta and pulmonary artery. Acetylcholine chloride was then injected into the aorta proximal to the occlusion in order to infuse it into the coronary system. Following completion of the operative procedure, atropine sulfate was similarly introduced into the aorta, perfused by manual compression through the heart, and then the superior caval and outflow occlusion were removed. As cardiac filling decreased, the inferior vena cava was disoccluded. For dogs of 10 to 15 Kg. body weight, 100 mg. of acetylcholine has been used. Human dosages have ranged from 75 to 100 mg. Perfused blood in either instance has been mixed with 100 mg. of acetylcholine per 500 ml. of blood immediately before use. Atropine sulfate, 0.6 mg., has been given for each 100 mg. of acetylcholine chloride except for that placed in the coronary *perfusate*.

EXPERIMENTAL BACKGROUND

The data relative to protection of the heart by inhibiting its action have been presented in detail elsewhere.[13] The story of the acetylcholine effect is summarized in the bar graph shown in Fig. 1. Twelve dogs were cooled and subjected first to one minute of occlusion alone, and then, following cardiac stabilization, a 10-minute period of occlusion with intracoronary acetylcholine (100 mg.) followed by 0.6 mg. atropine sulfate and disocclusion. The average normal cardiac rate of 164 fell to 71 with the hypothermia (25° C.), remained approximately the same with occlusion alone for the one minute, but fell to an average of 7 per minute during the 10 minutes under acetylcholine; shortly after atropine and disocclusion the average rate returned to 81. Surgical procedures induce added contractions, usually to a total of 10 per minute. Compared to the unmodified heart, the electrocardiogram in these animals shows less abnormality when return rhythm has been attained, and most striking the heart remains pink.

Perfusion of oxygenated blood through the coronary system maintains a good heart for cardiotomy.[14, 15] Only small amounts of oxygen are needed with the hypothermic metabolic inhibition. For example, at 25° C. a dog heart will extract 3 to 4 volumes per cent (aorta to coronary sinus) from a

perfusion of 1.5 ml. blood per Kg. body weight per minute. It is difficult to perfuse the small dog heart at less than 1 ml. per Kg. per minute for a prolonged period with a Sigmamotor pump system, but it is clear that even a 0.5 ml. per Kg. per minute will maintain a normal heart. If the heart has been stopped with acetylcholine, added perfusion will initiate cardiac contractions; therefore acetylcholine must be added to the perfusion system to maintain a quiet heart. Such perfusion, minimal quantitatively, still adds procedural problems and blood handling. It also produces a constant though small blood flow into the operative field.

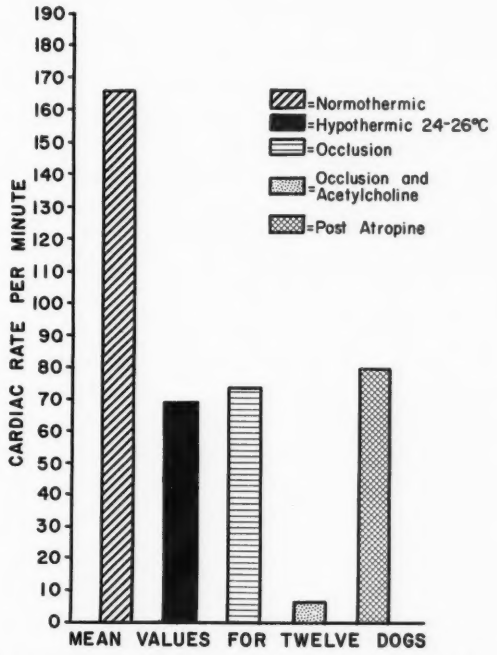

Fig. 1.—The effect of acetylcholine on cardiac rate in total circulatory occlusion.

Sixty-two dogs have undergone hypothermia with acetylcholine inhibition of heart activity for periods of time ranging from 5 to 37 minutes. Mortality, for the most part, has been associated with the more strenuous procedures. There has been a high incidence of fibrillation (29 in 62) in most instances following surgical procedures and the majority have been reversible. Intractable (or constantly recurring) fibrillation occurred in 9 dogs, and 4 of these were with direct coronary artery work.

Table I summarizes the data on these animals. General grouping of relative risk procedures has been done to simplify presentation. The average and range for temperature and occlusion time are given for each group. The longest time for occlusion was 37 minutes for a left atrial procedure. Operative deaths were primarily technical in the first two groups and from recurring

TABLE I ACETYLCHOLINE CARDIAC INHIBITION: OPEN CARDIAC SURGERY IN DOGS DURING HYPOTHERMIA

PROCEDURES	NUMBER OF DOGS	AVERAGE LOW TEMPERATURE (CENTIGRADE)	AVERAGE OCCLUSION TIME (MINUTES)	MORTALITY				LIVING, SACRIFICED, OR *PNEUMOTHORAX	VENTRICULAR FIBRILLATION	
				OPERATIVE	WARMING	RELATIVE TO SURGERY	TOTAL		REVERSIBLE	INTRACTABLE
Occlusion Right and left atriotomy Aortotomy	33	24.6° (22°-27°)	12 (5-37)	1	5	1	7	26	8	1
Right and left ventriculotomy	21	24.7° (22°-28°)	13 (9-19)	5	5	5	15	6	10	4
Open coronary artery	8	23.7° (20°-26.5°)	14 (9-21)	5	1	1	7	1	2	4
Total	62	24.8° (20°-28°)	13 (5-37)	11	11	7	29	33	20	29 9

*See text.

fibrillation in the coronary artery group. Deaths during rewarming were from hypotension, arrhythmia, and undiagnosed pneumothorax in the first group. Many in the ventricular group were from arrhythmias. Deaths "related to surgery" are from the effects of blood loss, arrhythmias, and 3 were from sudden reactions at the time of extubation following rewarming when the situation was otherwise quite well. Because of this, we now give 0.6 mg. atropine sulfate intravenously 10 to 15 minutes before extubation. Marked and persistent pneumothorax has appeared with the abandonment of atropine medication prior to cooling. There are additive effects from the restricted respiration used with the open chest and excessive inflation pressures used to re-expand the lungs. A few dogs, otherwise doing quite well, were found dead the morning after the day of surgery from the effects of pneumothorax. These have been included in the survival group (see Table I). The use of periodic tracheal suction during the cooling and warming periods, constant chest suction during warming, and avoidanec of excessive intratracheal pressures when expanding the lungs after the cardiac procedure, have obviated this complication. Excessive secretions and pneumothorax have not occurred in the few clinical cases.

Seven dogs had prior implantation of radioactive yttrium^{90} oxide pellets into a portion of the left ventricular myocardium or along the anterior descending branch of the left coronary artery. After the procedure all animals returned to a good rhythm and were sacrificed for the heart specimen. One animal was moderately hypotensive, but did not fail in a long waiting period before sacrificing. Compression was not used because the heart was to be preserved for study. This would suggest no exaggerated sensitivity of the damaged heart to hypothermia and cardiac inhibition during circulatory stasis.

The first group includes cardiac exclusion, right and left atriotomy, and ascending aortotomy. Although these can be carried out successfully under hypothermia alone, each was considerably safer and easier under these circumstances in our laboratory. Increase of the reasonable time limit for the intracardiac surgery was an immediate advantage. Most right atrial work was the production and closure of an interatrial septal defect, occasionally only the atriotomy was performed for the purpose of implanting radioactive yttrium^{90} oxide pellets into the atrioventricular nodal area. In the left atrium two-thirds closure of the mitral valve by direct suture was the only operation; however, the exposure is surprisingly good and any combined valve and septum or similar work could be done. Only a mock procedure on the aortic valve was performed from the open ascending aorta. In the dog exposure of the coronary orifices for any direct work is only fair from this site.

An interventricular septal defect was made and closed by either suture alone or suture with an Ivalon sponge in the right ventriculotomy group. A limited endocardial resection was performed in the animals having left ventriculotomy. The operative deaths were usually technical, such as making a high septal incision and cutting the aortic valve or interfering with the right conduction bundle; these animals developed intractable ventricular

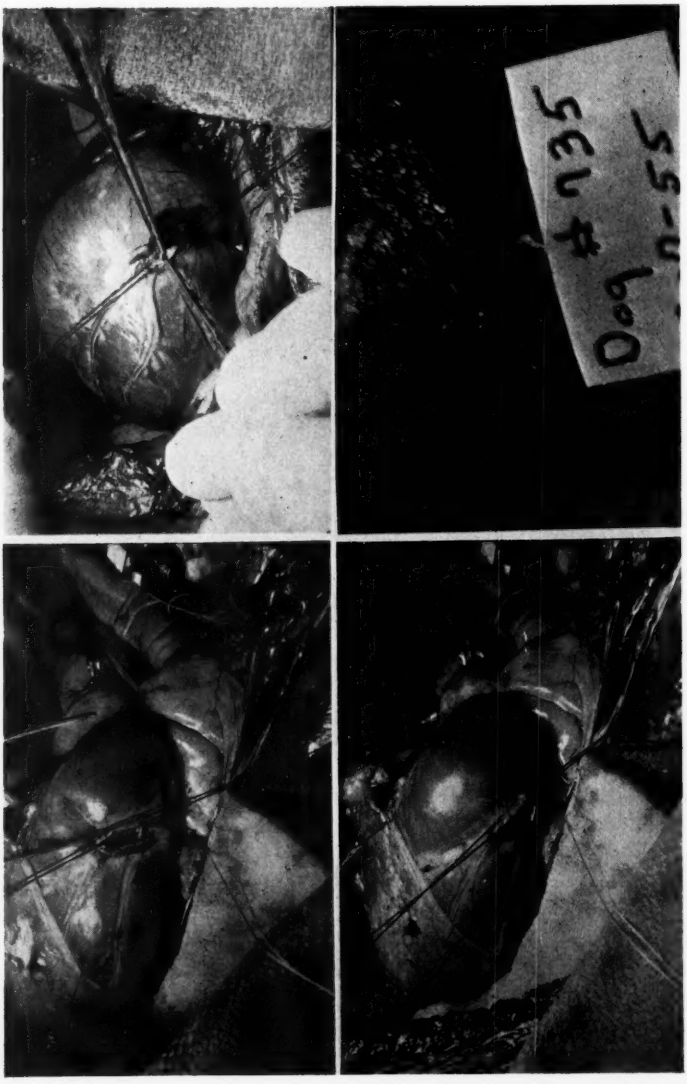

FIG. 2.—*Upper left:* The dissected anterior descending branch of the left coronary artery is open and a mock endarterectomy is being performed. *Upper right:* the orifice of the coronary artery is being held open. *Lower left:* Interrupted suture closure. *Lower right:* Probe readily passes through the site of the closure of the coronary artery at post mortem after dog was sacrificed.

fibrillation. We now use the low-septal, thick, muscular area to avoid these variables, but it is, unfortunately, simpler and not the site for the predominant clinical ventricular septal defect. This group was extremely discouraging with 15 of the 21 not surviving and 14 having ventricular fibrillation. Although the impression during the procedure was that it was a good system, and knowing that during this period of the study a series of sick (distemper, etc.) and dogs fresh from the pound were used of necessity, these findings have precluded moving the method alone to clinical cases.

In 8 hypothermic dogs, a segment of the anterior descending branch of the left coronary artery was dissected free over a 2 to 2.5 cm. length, then the usual procedure of cardiac exclusion and acetylcholine injection was accomplished and direct procedures performed on the opened artery. Incision, mock endarterectomy, and closure of the coronary artery (Fig. 2) or insertion of a by-pass carotid autograft previously placed on as proximal an aortic site as possible was performed. After reinstitution of the circulation, there is a short period of coronary insufficiency over the area supplied by the anterior descending branch of the left coronary artery. Dissociated ventricular contractions occur; and fibrillation ensues if the time period is prolonged. Following support with cardiac compression for a time, the ischemic area of the heart begins to change from blue to pink and a good rhythm will appear, or if fibrillation has intervened, defibrillation can be accomplished. Suspecting coronary spasm as a factor in this period of insufficiency the effect of local anesthetic agents and papaverine hydrochloride is being studied.

Although these procedures can be done on the active heart, it was obviously easier with the dormant heart, and the methods would probably be more reproducible. Suturing has been done with No. 6-0 silk and only a minute edge of vessel can be used in the closure to prevent partial occlusion. Interrupted techniques are most satisfactory. Blood flow into the distal coronary artery has been present in all eight preparations, although obviously diminished in some of the early ones. These techniques can be partially mimicked on rabbit iliac and femoral vessels.

CLINICAL EXPERIENCE

Open heart surgery in human beings has been limited to a small number of patients, usually of considerable risk. Each of the 5 cases has had a different lesion: Ostium secundum and ostium primum interatrial defects, atrioventricularis communis, aortic stenosis, and a unique form of interventricular septal defect.

The unspectacular end results and other data are given in Table II. The first 4 patients were handled with hypothermia and acetylcholine inhibition of the heart. The ventriculotomy (Case 5) was performed with the addition of a coronary perfusion of oxygenated blood at the rate of 2 ml. per Kg. body weight per minute containing 100 mg. acetylcholine per 500 ml. perfusate.

All hearts were slowed by the acetylcholine; however, the huge heart in the patient with the aortic valvular stenosis started recovering from

TABLE II. ACETYLCHOLINE CARDIAC INHIBITION:

PATIENT	DIAGNOSIS	PROBLEM	PROCEDURE	TEMPERATURE (CENTIGRADE)
16 years ♀	Ostium primum Interatrial defect	Bacterial endocarditis, 2 × Cardiac failure Left-to-right shunt	Suture closure	23°
4 years ♀	Ostium secundum Interatrial defect	Repeated pneumonias and infections Moderate cardiomegaly Left-to-right shunt	Suture closure	22.5°
1 year ♂	Atrioventricularis communis	Cardiac failure Retardation	Suture closure	23°
30 years ♂	Aortic valvular stenosis	Coronary insufficiency Cerebral ischemia	Open aortic valvulotomy	26°
13 years ♀	Corrected transposition aortic chamber ⊂⊃ common ventricle	Cyanosis Cardiac failure Respiratory distress Retardation Huge shunt	Incomplete formation of interventricular septum with Ivalon sponge	24° Perfusion of coronary arteries

the inhibition in about three minutes. Motion effects prevented accurate electrocardiographic counting of contractions, but usually there were 2 or 3 to 10 contractions per minute. Reversal was accomplished in all but the third case. An irreversible standstill with a heart that suggested a potassium-arrested heart occurred near the end of the procedure, and only calcium ions produced slight activity with some tone. All efforts at resuscitation were ineffective. Autopsy demonstrated that a technically poor closure had been obtained. With closure of the ostium primum interatrial defect it was difficult to fill the left heart and air embolism was encountered with ventricular fibrillation at disocclusion. Defibrillation was accomplished.

At no time did these patients evidence arrhythmia during the cooling period. The blood in the surgical field was visibly well oxygenated and the hearts were quite pink at cardiotomy. In the third case continuously recorded ear oximeter values showed 91 to 93 per cent blood oxygen saturation during cooling and bilateral thoracotomy. Following restitution of circulation the saturation was about 80 per cent and remained at 85 to 90 per cent during warming.

From a technical point of view the work in the first 4 cases was done in a dry, quiet field. In the ostium primum heart it was possible to do quite careful suturing on the septal brim above the nodal and conduction tissue, and this patient has shown no rhythm disturbance in the six months since surgery. The aortic valvulotomy would not have been too difficult with any method, but under these circumstances a good valvulotomy without regurgitation, cusp damage, or embolic danger was easily performed, and the immediately modified murmur disappeared entirely by the fourth postoperative day.

OPEN CARDIAC SURGERY IN HUMAN BEINGS DURING HYPOTHERMIA

CARDIAC EXCLUSION TIME (MINUTES)	ACETYLCHOLINE (MG.)	COOLING TIME (HOURS)	WARMING TIME (HOURS)	RHYTHM	RESULTS REMARKS
13½	100	6⅔	4	Ventricular fibrillation (air embolism)	Grossly complete closure; living and well at 6 months; no arrhythmias (operation 11/29/55)
9	80	6½	3¼	Normal	Grossly complete closure; living and well at 5 months
17	75	2⅔	—	Cardiac standstill	Operative death; cause of standstill undetermined; technically a poor closure
4½	100	7	5½	Normal	Cerebral edema 1 day, murmur gone by 4 days; died 7 days; massive pulmonary embolus; autopsy showed excellent valvulotomy
22	100 +	4½	2½ (Incomplete)	Normal	Died while warming (34°) from bleeding due to coagulation defect

In the fifth case where coronary perfusion was performed, the heart was quiet, but the presence of the returning blood proved strikingly different from the other bloodless cardiotomies. With minimal contractions and the low temperature it was conspicuous that the cardiac venous blood was red shortly after the perfusion was started (at only 2 ml. blood per Kg. body weight per minute).

DISCUSSION

Open heart surgery under hypothermia has been a reality because of the work of Bigelow,[1] Lewis,[3] and Swan,[4] and their co-workers. These studies are complementary to existing techniques and are intended for further protection of the heart and for increasing safe operative time. From an experimental point of view, it is suggestive that some added antifibrillatory drug or mechanism could be added for at least the more difficult and prolonged procedures.

On the one side investigators have found that a small amount of coronary (and brain) perfusion of oxygenated blood increases the safety of hypothermia for cardiac procedures and, on the other, decreased blood flows are being used with normal temperature extracorporal pump oxygenating systems.[16] We might eventually expect a common meeting place for both methods with moderate cooling and extremely low flow rates from an extracorporal circuit. Short cooling time, long operative time, and simplified apparatus would result. Inhibition of cardiac activity would also be additive under these circumstances. However, open procedures upon and eventually replacement of the aortic valve seem possible only with hypothermia. Direct

coronary work may also be found to be dependent upon a quiet heart with circulatory stasis, a situation which has been demonstrated to be possible with this modification of hypothermic surgery.

CONCLUSIONS

1. Intracoronary acetylcholine markedly inhibits cardiac activity during cardiac exclusion under hypothermia. Its effect is readily reversible with atropine.

2. Surgical procedures in the four cardiac chambers, the open aorta, and on the coronary arteries can be performed in dogs with this method.

3. Direct vision atrial and aortic cardiac surgery have been performed in human beings with acetylcholine inhibition of cardiac activity under hypothermia.

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DISCUSSION

DR. CONRAD R. LAM, Detroit, Mich.—A year ago, Dr. Geoghegan, Dr. Lepore, and I presented before this Association a paper entitled "Induced Cardiac Arrest for Intracardiac Surgical Procedures" (J. Thoracic Surg. 30: 620, 1955). You will recall that we used potassium chloride to produce this arrest, and the recovery phase was almost invariably accompanied by ventricular fibrillation. We immediately began to seek a way to avoid this complication and last November we began to use acetylcholine.

(slide) This is the record of one of the animals. We see the normal aortic pressure and Lead II of the electrocardiogram. This is the record taken at the time of vena caval occlusion and after the acetylcholine was injected; the heart was stopped at this point. Here we have complete asystole. At this point the coronaries were perfused with oxygenated blood, and 3 minutes later a slow contraction occurs, then 30 minutes later a normal contraction. I felt we should wait for the availability of an oxygenator before trying this on a patient and for that reason there was some delay.

(slide) This is the electrocardiographic record of a 14-pound patient, 13 months old, with an interventricular defect, who had acetylcholine arrest of the heart for 15 minutes. Here is the normal electrocardiogram. This is the record of 15 minutes of arrest and 30 seconds after the clamp was removed from the aorta and the oxygenated blood allowed to flow in. You see the first contraction, the second one, after one minute, 2 minutes, and the record on the first postoperative day.

(slide) This shows the picture of this boy on the second postoperative day. The opening in the ventricle was closed with a perfectly dry field and a perfectly still heart. The combination of a suitable oxygenator plus arrest with some drug such as acetylcholine, seems to be the answer to this form of intracardiac surgery.

DR. HENRY SWAN, II, Denver, Colo.—Late in 1954, on the basis of our laboratory experience, we began to use clinically the relatively short-acting anticholinesterase prostigmine, which we gave by coronary perfusion after circulatory occlusion had been set up. We now have had the opportunity to observe the action of this agent on about 75 patients, and we continue to believe that it is valuable. Prostigmine, in the doses that we use, markedly slows the heart but does not actually stop it. Heart rates of the magnitude of from 3 to 25 a minute persist throughout the operative procedure. We felt at first, and I am interested in hearing of the work this morning, that acetylcholine would have too short an action because it is so rapidly destroyed. Yet on the basis of what we have heard today I believe this is not necessarily true. Following prostigmine, as Dr. Lam has said, the heart starts readily again when circulation is restored.

With regard to the use of hypothermia alone, we have been gradually exploring the perimeters of that as a safe technique for opening the heart, and we must of course admit that the heart does undergo a continuing and progressive hypoxia during the period of circulatory occlusion. The protection of hypothermia is relative, of course, and is not absolute, so that we cannot expect it to be of indefinite duration with or without stopping the heart. We have gradually come to use a lesser range of hypothermia than when we began, because we found that we did not encounter ventricular fibrillation in these patients under the temperature of 28° C., rectal temperature. So that we have gradually come to use the range from about 28° to 31° C., and we feel that the brain will be protected for periods up to 12 or 15 minutes at this temperature; we think that 10 is fairly safe and 8 very safe indeed. We have had no cerebral damage in using this range.

Currently, then, we are recommending that the range of temperature for clinical application of hypothermia alone be in the neighborhood of 28° to 31° C. because of the relative absence of serious arrhythmias, with occlusion times of the heart not to exceed 8 minutes, and with the heart under the influence of an anticholinesterase with the coronary circulation occluded.

DR. PETER V. MOULDER, Chicago, Ill. (Closing).—I should like to show one slide that brings out a point relative to the discussion of Dr. Swan. The slide demonstrates the effect of cardiac occlusion for 50 minutes. Before occlusion there is a good pressure, normal electrocardiogram; after occlusion, no pressure; then following intracoronary acetylcholine (100 mg.) the electrocardiogram shows cardiac arrest, the next partition shows, at 10, 30, and 50 minutes, no electrical activity (or cardiac contractions). The last part shows 5 or 6 minutes after disocclusion with a relatively normal electrocardiogram and a good effective pressure. This was one of those fortunate experiments in which virtually no contractions occurred during the entire 50 minutes. The heart will be resuscitated without the atropine, responding to the filling of the heart with blood and coronary blood flow, but a ventricular or nodal rhythm will persist for a considerable period. The atropine produces rapid reversion to a normal sinus mechanism.

BUCCAL AND INTRAMUSCULAR TRYPSIN IN RESPIRATORY TRACT INFECTION

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MANY investigators have commented on the virulence-potentiating influence of viscid, sticky respiratory secretions.[1-4] During the past five years reports have been published describing favorable effects of various enzyme preparations on lesions in which thick, tenacious, purulent, or mucopurulent exudates constituted an obstacle to healing.[5, 6] These enzymes were either of streptococcal (streptokinase and streptodornase) or pancreatic (crystalline trypsin) origin. Owing to antigenicity, the aerosol use of streptococcal enzymes is limited. Trypsin, however, has been successfully employed by several groups on the hemothorax and empyemas of varying etiology,[7] poliomyelitis patients with tracheotomy,[8] and respiratory conditions with thick sputum.[9] In these studies, trypsin was instilled intrapleurally or administered by aerosol inhalation. In 1952, one group reported disappearance of the fibrinopurulent zone which lined infected bronchopleural fistulas following use of intravenous trypsin.[10] In 1954, another investigator used trypsin intramuscularly and observed liquefaction of sputum and rapid diminution of cough in patients with acute or chronic bronchitis and bronchial asthma.[11]

When active proteolytic enzymes were observed to penetrate connective tissue in recent studies, the buccal route for administering trypsin became a distinct possibility.[12-14] Reduction of edema and prompt subsidence of other signs and symptoms of inflammation following buccal trypsin has already been reported.[15, 16] In the present paper, clinical observations are described which document the efficacy of trypsin tablets given buccally, combined with intramuscular trypsin (Parenzyme), in rapidly controlling the signs and symptoms of respiratory infection.

METHODS AND PROCEDURE

The study was comprised of 43 patients.

TABLE I. DIAGNOSIS IN 43 PATIENTS

DIAGNOSIS	NUMBER OF PATIENTS
Acute bronchitis	14
Chronic bronchitis	9
Chronic bronchiectasis	13
Unresolved pneumonia	4
Bronchopleural fistula	3

From The New York Medical College-Metropolitan Medical Center, Metropolitan Hospital Division, New York City.
Received for publication Nov. 30, 1955.

The prime prerequisite for acceptance in this investigation was evidence of inflammatory disease of the respiratory tract associated with viscid, sticky secretions. Quantitative measurements must be made in order to evaluate the influence of any therapeutic agent in respiratory tract infection. While several clinical features were studied, the following criteria were considered most objective and important for appraisal in this study: (1) sputum or exudate viscosity, (2) quantity of sputum raised, (3) extent and character of the cough, (4) effect upon granulation tissue, (5) vital capacity, and (6) general systemic effects (weight, sleep, appetite, sense of well-being). Viscosity was measured by the method of Harris, Abrams, and Harris.[17]

Parenzyme,* a suspension of crystalline trypsin in sesame oil, was given once daily in 0.5 c.c. intramuscular doses containing 2.5 mg. of trypsin.

Buccal trypsin, containing 2.5 mg. crystalline trypsin, was administered every three, four, or six hours for periods varying from three days to twenty-five weeks. During the first week of treatment Parenzyme and buccal tablets were used concomitantly. For maintenance, only buccal tablets were used.

Side Effects.—About one-third of the patients on buccal trypsin complained of a tingling sensation along the tongue edge, or at the site of buccal application. However, this complaint was much less frequent on the second treatment day and was practically gone by the third day. Treatment had to be discontinued in only 2 patients because of mouth soreness. It is of interest that each of these 2 had previously been treated vigorously with intramuscular trypsin (Parenzyme) and had developed sensitivity reactions.

RESULTS

In general, the results were consistent with physiologic alterations associated with the subsidence and reversal of inflammation. These changes included: (1) Decreased viscosity of sputum and/or purulent exudates. (2) For the first few treatment days there usually appeared an increase in the quantity of sputum raised. This effect was probably related to digestion of mucus with reduction in viscosity and improved bronchial ciliary effect. (3) After two or three days the cough became much more loose. After four to five days, coughing decreased. (4) Granulation tissue growth was accelerated in patients with bronchial ulceration or infected bronchopleural fistulas. This was confirmed bronchoscopically. (5) Changes in vital capacity varied from slight to marked. This effect was most marked in patients with long-standing bronchiectasis. (6) With few exceptions, following prolonged therapy with the combination of Parenzyme and buccal trypsin there was an increase in weight, improved sleep, better appetite and feeling of well-being.

CASE REPORTS

1. *Acute Bronchitis.*

J. M., a 17-year-old student, complained of chilliness, malaise, pains in the back and muscles, headache, coryza, dry scratchy throat, and voice huskiness. The temperature was 101° F., white blood count was 12,500. Twenty-four hours later, a dry irritative nonproductive

*Parenzyme was supplied by the National Drug Company, Philadelphia, Pa.

cough developed, associated with substernal soreness. The next day some scanty viscid sputum was raised with difficulty. On physical examination, scattered squeaking, and occasional sonorous, râles were heard. Crackling râles were present at both bases. The breath sounds were bronchovesicular.

Forty-eight hours after the onset of this illness, trypsin therapy was instituted in the following manner: one-half cubic centimeter of Parenzyme was given intramuscularly daily, plus one buccal trypsin tablet every four hours. When examined the next day the patient appeared far more comfortable. The temperature was normal, the cough was much softer, the sputum was copious and easily raised. Therapy was discontinued after another twenty-four hours.

2. *Chronic Bronchitis.*

N. B., a 34-year-old housewife, had a dry, irritative cough for eight years, which became aggravated by cold weather or following upper respiratory infections. In the past year, following an episode of severe bronchopneumonia, the coughing became worse, sputum became scanty and mucopurulent. There was an occasional episode of paroxysmal coughing of several minutes' duration, persisting until sputum was raised. On physical examination, chest expansion was diminished. Scattered areas of sonorous, squeaking, moist râles were heard, which cleared after a vigorous cough.

Treatment consisted of one-half cubic centimeter of Parenzyme intramuscularly plus one buccal trypsin tablet every four hours. Four days later the following changes were recorded: (1) the sputum was thinner, more abundant, and easily raised, (2) the cough was more loose, (3) only an occasional crackling râle was heard, and (4) the patient felt considerably improved and was eating and sleeping better. After the first week, intramuscular Parenzyme therapy was discontinued and the patient was maintained on one buccal tablet, 3 times a day. This regimen was discontinued after four months, when the patient stated she coughed only occasionally and chest examination was negative.

3. *Chronic Bronchiectasis.*

P. M., a 37-year-old Puerto Rican man, was admitted to Metropolitan Hospital because of shortness of breath and ankle edema of three days' duration. He had been coughing for eight years, occasionally expectorating a large amount of sputum. At various hospitals he had been told he had bronchial asthma. He had been followed in an outpatient department of an outside hospital with ephedrine tablets, and had improved until three days prior to this admission. On physical examination, the temperature was 99° F., apex rate 108, radial rate 78, blood pressure 105/60. He appeared malnourished and dyspneic. A fetid odor permeated his room. The lungs were emphysematous, with hyperresonance noted in both lung fields. Many moist râles were present in both bases. There was a sinus tachycardia on ECG. Chest film showed extensive bilateral bronchiectasis. The liver was 1½ fingerbreadths below the costal margin. A three plus ankle edema was present. Prominent clubbing of the fingers and toes was evident.

Laboratory findings: Urine specific gravity was 1.020, and was negative for sugar, pus, or albumin. Blood urea nitrogen was 16 mg. per cent, albumin-globulin ratio was 2.8/3.8; total protein, 6.6; cephalin flocculation test was negative. Thymol turbidity test was 1.4 units, and hemoglobin, 13.5 Gm. White blood count was 8,100 to 17,200; eosinophil, 2 per cent; red blood count, 4.75 million. A Mazzini test was negative. Sputum cultures revealed intermediate coliform organisms, sensitive to Aureomycin, Chloromycetin, and Terramycin. *Proteus vulgaris* and *Alcaligenes faecalis* organisms were recovered. Sedimentation rate was 1.0 mm. per 15 minutes and 0.0 mm. per 15 minutes. ECG showed right ventricular preponderance.

For the first two weeks of his present hospital stay, treatment consisting of Aureomycin, penicillin, and Chloromycetin, was ineffectual. He then was placed on buccal trypsin therapy, one tablet every three hours for three days, and then every six hours for maintenance.

After seventy-two hours of buccal trypsin therapy the following changes occurred: (1) the fetid odor disappeared, (2) coughing was increased, but more loose, (3) the sputum

was much thinner and more abundant, and (4) expectoration was easier. On postural drainage large quantities of mucopurulent material were evacuated.

This patient maintained the above level of improvement while on buccal trypsin for an additional two weeks. Buccal trypsin therapy was then terminated. After ten days without trypsin, all the previous symptoms gradually returned.

4. *Bronchopleural Fisula.*

L. N., a 24-year-old Puerto Rican seamstress, was referred to the hospital from the chest clinic with a diagnosis of chronic pneumonitis and lung abscess involving the left lower lobe. A lobectomy was performed, but the postoperative course was complicated by a profuse purulent discharge accompanying diffuse cellulitis of the operative site. This was followed in three weeks by a bronchopleural fistula. Purulent drainage was profuse and impossible to control with antibiotics, local lavages, and topically applied Varidase (streptokinase). Trypsin therapy was started consisting of two 2.5 mg. Parenzyme injections plus one buccal trypsin tablet every four hours.

Twenty-four hours later the fistulous discharge was considerably thinner and less abundant. Forty-eight hours later, there was definite decrease in intensity of the redness involving the entire fistulous tract. At the end of one week maintenance trypsin therapy was instituted with one buccal tablet every four hours. Two weeks later the drainage from the wound was very scanty and mucoid in character. Three weeks later the patient was discharged, at which time the previously necrotic material lining the fistulous tract was replaced by healthy, abundant granulating tissue.

DISCUSSION

Except for two reports on parenteral trypsin,[10, 11] all previous studies on enzyme therapy in respiratory tract infection were based upon intrapleural or aerosol administration.[1-9] In this study, an intramuscular preparation (Parenzyme) and buccal trypsin tablets were employed. The difference between parenteral (Parenzyme) and topical (aerosol) given trypsin are significant. An average single dose of trypsin given by nebulizer is 100 mg.; in one report the single dose was 800 mg. of trypsin.[1] Each dose of Parenzyme contains only 2.5 mg. of trypsin; the buccal tablet also contains 2.5 mg. trypsin.

Enzyme dosage in topical (aerosol) therapy is high since there is direct enzyme-substrate interaction, and the extent of protein substrate depolymerization is a direct function of the quantity of enzyme introduced. The dose of parenterally given trypsin on the other hand is small, since the physiologic action of parenteral trypsin seems to be activation of the patient's own proteolytic enzyme system, i.e., the conversion of precursor "plasminogen" into the active enzyme "plasmin."[18, 19] The enzyme-protein substrate complex following parenteral trypsin is a *plasmin*-protein substrate interaction, unlike the *trypsin*-protein substrate reaction mixture which characterizes aerosol administration.[20]

Since very small trypsin quantities constitute each dose of parenteral trypsin, the rather unpleasant and occasionally serious consequences of massive trypsin aerosol doses are avoided. At no time in this study did we encounter any of the following side effects associated with aerosol enzyme therapy; dyspnea, chills, fever, hoarseness, nasal and eyelid irritation.

In order to understand the physiologic role of trypsin in reversing inflammation, one should think in terms of a dynamic equilibrium between proteolytic enzymes and protein macromolecules.[21] From time immemorial, it was recognized that an area of acute localized inflammation contained highly viscous

exudates. Recent animal studies[22] suggest that following parenterally given trypsin, there is correction of a proteolytic enzyme-protein macromolecular substrate imbalance in the area of local tissue injury. There then follows reduction in viscosity of edema fluid,[23, 24] purulent exudates and lymph, with rapid cleansing of necrotic debris. Ehrich[25] defines inflammation as a "disturbance in homeostasis." Our studies suggest that one of the fundamental homeostatic disturbances in inflammation is the impaired proleolytic enzyme-protein substrate equilibrium. In keeping with this viewpoint, clinical observations made in this study suggest that patients with signs and symptoms of respiratory tract infection benefit from trypsin therapy following enzymatic modification of excessively long chained protein macromolecules in the exudates of inflamed bronchial or pulmonary tissue. This would explain the reduced viscosity, tenacity, and inspissation of respiratory secretion following buccal trypsin and Parenzyme therapy.

It appears that buccally and intramuscularly given trypsin adequately corrects fundamental proteolytic enzyme-protein substrate abnormalities in respiratory tract infection, and as a direct consequence there is a significant decrease in the viscosity and tenacity of respiratory secretions.

SUMMARY AND CONCLUSIONS

In clinical conditions associated with thick, tenacious, respiratory secretions, trypsin therapy (intramuscular Parenzyme combined with buccal trypsin tablets) has the following effects:

1. The sputum becomes thinner, more abundant, easier to raise.
2. The cough becomes more loose, more productive.
3. Accelerated granulation occurs in bronchial ulcerations and bronchopleural fistulous tracts.
4. In chronically ill patients, there appears weight gain, improved appetite, improved sleep and sense of well-being.
5. Acutely ill patients show rapid resolution of inflammation, with early subsidence of cough and substernal burning.
6. In this study, intramuscular trypsin (Parenzyme) and buccal trypsin were used. For long-term maintenance therapy, buccal trypsin alone was employed. The incidence of side effects was low.

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FUNCTIONAL ANATOMY OF THE NORMAL MITRAL VALVE

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THE opening of a new field of surgical endeavor often arouses interest in the detailed anatomy of the involved part of the body. As a result of such studies, current notions may be so changed and extended so as to understand better the morphologic structures of the organ and to provide a scientific basis for its function. The impetus given to mitral valve surgery in the course of the last few years has prompted a thorough revision of our knowledge concerning the anatomy of the normal mitral valve. The classical description of the mitral valve found in the textbooks of anatomy is inadequate for the need of the cardiac surgeon. Similarly, the importance of the valvular structures and the myocardium in the mechanism of valve closure requires a new appraisal in view of recent observations.

It is the purpose of this study to focus attention upon certain anatomic features of the normal mitral valve and their significance in the mechanism of valve closure.

MATERIAL AND METHODS

One hundred and five normal hearts were studied. They were from 60 men and 45 women between the ages of 19 and 65 years. The specimens were, for the great majority, preserved in 4 per cent solution of formaldehyde. They were chosen from cases in which there was no evidence of cardiac disease, except for a small number that exhibited a moderate degree of coronary arteriosclerosis.

In each heart a detailed examination was made of the valve leaflets, mitral ring, chordae tendineae, and papillary muscles. Measurements of various elements associated with the valve apparatus were taken, namely, (1) the diameters and the circumferences of the orifice, (2) the surface area of all valve leaflets and junctional tissue, (3) the height of each single valve leaflet measured in the central portion, from the apex to base, (4) the breadth of the single valve leaflet at the line of insertion at the valve ring, and (5) the depth, that is, the perpendicular measurement from the free edge to the valve ring, of the junctional tissue when this had not become differentiated into valve leaflets.

Received for publication Dec. 5, 1955.

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A pair of dividers and a metric ruler were used for the linear measurements. The surface area was obtained by planimetric integration of the valvular tissue, carefully divided with tiny scissors from its attachments to the valve ring and to the chordae tendineae. This was done in 16 fresh hearts; 8 female, and 8 male specimens. The greatest care was exercised in preserving the dimensional figures found in situ when calculating the valvular tissue surface area. In other words, during the process of planimetric integration, we tried to neutralize the overstretching tendency of the excised valvular tissue by keeping the same figures as far as circumference, the height and the breadth of the leaflets, and the depth of junctional tissue were concerned.

THE NORMAL MITRAL VALVE APPARATUS

The normal mitral valve apparatus is composed of various structures including the mitral ring, the valve proper, the chordae tendineae, and the papillary muscles.

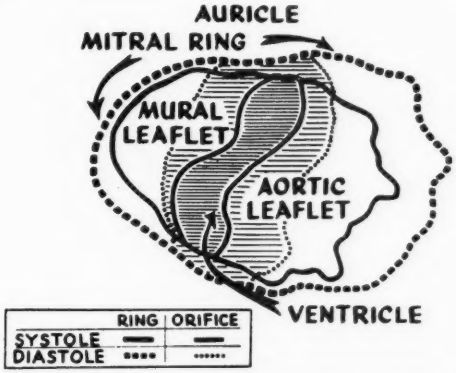


Fig. 1.—Diagram demonstrates the sphincterlike action of mitral ring and changes in contour of lumen in systole and diastole. Under experimental conditions the atrium and the ventricle are bloodless. "Inspite of this and other deviations from normal it is remarkable to see how much valvular and ring function actually takes place" (Hurwitt). (Courtesy The American Journal of Medicine, February, 1953.)

The Mitral Ring.—The mitral (atrioventricular) ring or annulus is an important part of the skeleton of the heart.[1] It is an anteriorly incomplete, circular, and fibroelastic structure. It represents the dividing line between the atrial and ventricular musculature from the eighth week of intrauterine life on and appears in the embryonic heart as a result of the crowding together of the connective framework of the organ. The ring's upper border is the point of origin of atrial muscular fibers and its lower border is the point of origin of the ventricular musculature. It has recently been shown that the atrioventricular annulus decreases its diameter during each systolic contraction[2] (Fig. 1). This event, which takes an effective part in the closure of the normal mitral valve, is probably the result of the systolic contraction of the deep bulbo- and sinospiral muscles with the superficial bulbospiral muscle assisting in a minor role. In the experimental animal, the impression is gained that the orifice is completely obstructed during the late stage of the cardiac systole by the sphincterlike action of the annulus.

TABLE I. MEASUREMENTS (IN CM.) OF NORMAL MITRAL VALVES (105 HEARTS)

STRUCTURES MEASURED	MEN (60 SUBJECTS)				WOMEN (45 SUBJECTS)			
	HEIGHT		BREADTH		HEIGHT		BREADTH	
	AVERAGE	RANGE	AVERAGE	RANGE	AVERAGE	RANGE	AVERAGE	RANGE
Aortic leaflet	2.4	3.2 – 1.9	3.7	4.5 – 2.5	2.2	2.7 – 1.8	3.3	4.2 – 2.4
Ventricular leaflet	1.4	2.5 – 1.0	3.3	4.1 – 2.5	1.2	2.4 – 0.8	3.0	3.6 – 2.3
Anterior accessory leaflet	1.1	1.8 – 0.8	1.5	1.8 – 1.1	1.0	1.3 – 0.7	1.2	1.6 – 1.0
Posterior accessory leaflet	0.9	1.2 – 0.6	1.1	1.5 – 0.8	0.9	1.0 – 0.7	0.8	1.2 – 0.7
Anterior junctional tissue	0.8	1.2 – 0.6	1.7	2.4 – 0.7	0.7	1.1 – 0.6	1.5	2.1 – 0.7
Posterior junctional tissue	0.7	0.9 – 0.5	1.3	1.8 – 0.7	0.6	0.8 – 0.4	1.2	1.6 – 0.7
Circumference of valve ring			10.0	11.5 – 8.5			9.0	10.5 – 8.0

The outer aspect of the mitral annulus constitutes the deepest part of the atrioventricular groove on the external surface of the heart. The mitral valve takes origin as a continuous veil from the inner aspect of the ring and inserts around the entire circumference of the mitral orifice.

In this study we found that the circumference of the mitral annulus was in average 10 cm. (range: 8.5 to 11.5 cm.) in the male specimen, and 9 cm. (range: 8 to 10.5 cm.) in the female specimen (Table I). The readings obtained were very seldom found at variance with these figures.

Fig. 2.—Photograph of a human mitral valve showing anterior and posterior accessory leaflets. Two big arrows indicate the position of these minor cusps. The small arrow points to the ventricular leaflet. (Institute of Pathologic Anatomy, University of Bari Medical School, Italy, Autopsy No. 2597.)

The Mitral Valve Proper.—The mitral valve is represented by a continuous veil of valvular tissue attached as a muff to the entire circumference of the atrioventricular annulus. Its free edge is split by indentations, none of which reaches the mitral annulus. These clefts divide the valvular tissue into two major leaflets which are always present and into two minor accessory cusps not invariably present. These minor cusps, when present, are at the area of the junctional tissue (Fig. 2).

The valve tissue consists of a fibroelastic texture covered on the atrial and ventricular aspect by a coat of endocardium. The so-called fibrous skeleton which gives strength and shape to the valve is furnished by a layer of connective tissue protruding from the inner aspect of the mitral ring. Important contributions to the valve-supporting framework are the chordal insertions. Rusted and his associates[3] noted that the chordal insertions passed through the substance of the leaflet for a considerable distance. This particular arrangement, as pointed out by the Mayo Clinic group, is often seen on the transilluminated posterolateral leaflet, but more often a fibrous band running along the margin of closure is seen in this leaflet. This fibrous structure can be considered as the point of insertion of the chordae. Neither the junctional tissue nor other additional valve leaflets show any such arrangement of their connective layers.

The two major cusps are attached to the ring in such a way as to be in anteromedial and posterolateral locations. The anteromedial cusp has been referred to as the anteromedial, aortic, septal or greater leaflet. The posterolateral has been designated as the posterolateral, ventricular or lesser leaflet. The major axis of the mitral orifice is consequently directed obliquely forward from right to left.

The Anteromedial or Aortic Leaflet.—The aortic leaflet is the most important from the anatomic as well as the physiologic standpoint. Table I shows the linear measurements of the various valve leaflets. Table II lists the surface measurements of the same structures, obtained by planimetric integration of the removed valvular tissue. The aortic cusp is by far the largest. It exceeds every other leaflet in height and breadth at the mitral ring. Its surface area gives a better idea of the importance of this cusp, because it is equal to almost one-half of all valvular tissue surface area.

TABLE II. MEASUREMENTS (IN MM.²) OF NORMAL MITRAL VALVE (16 HEARTS)

STRUCTURES MEASURED	MEN (8 SUBJECTS)		WOMEN (8 SUBJECTS)	
	AVERAGE	RANGE	AVERAGE	RANGE
Aortic leaflet	651	833 – 427	563	714 – 413
Ventricular leaflet	384	532 – 270	334	456 – 413
Anterior accessory leaflet	227	257 – 193	203	220 – 183
Posterior accessory leaflet	136	148 – 110	120	128 – 112
Anterior junctional tissue	171	200 – 129	144	171 – 125
Posterior junctional tissue	92	110 – 70	78	94 – 67
Valvular tissue area	1398	1770 – 1000	1220	1518 – 970
Mitral orifice area	793	1020 – 572	642	875 – 490

The anteromedial cusp is roughly triangular in shape and, in our experience, its free edge has never been found split.

It is the only dividing structure between the mitral and the aortic orifice. Directly inferior to the aortic canal, it constitutes an integral part of the outflow tract of the left ventricle. Due to this anatomic location, a considerable portion of its function is believed to be the direction of the flow of blood toward the aorta. This has been described by Harken[4, 5] as the aortic baffle. In other words, the leaflet apparently acts as a watershed which deflects the blood toward the aorta in the ejection phase of the ventricular contraction.

Close anatomic observation of the normal heart as well as experimental investigation of the valvular function would not be in favor of this view. The leaflet has the greatest importance in the closure of the mitral valve, but it has no baffling action on the blood flow. Indeed, the blood driven forcefully from the inflow into the outflow tract has no other outlet but the aortic orifice, since the mitral valve is, at this stage of the systole, hydraulically closed. The physiologic lines of progression upon which the blood is forced out into the aorta run directly from the apex of the heart to the aortic canal. The contribution of the anteromedial leaflet to the formation of these lines of direction is certainly not greater than that of the interventricular septum or the anterior left ventricular wall. The last mentioned two structures together with the septal cusp constitute the walls of the outflow tract of the left ventricle. If a defect is produced in the aortic leaflet, as it was in the case of the famous patient of Dr. Adam,[6] or as it is possible to do in experimental surgery, a great valvular incompetence ensues since here there are no compensatory mechanisms likely to limit the mitral reflux. Likewise, a defect of the interventricular septum will permit an escape of blood into the right ventricle. The two situations, the mitral reflux and the escape of blood through an interventricular septal defect, are indeed dynamically analogous since both are governed mainly by the intracavitary pressure. On the other hand, the muscular fibers of the outflow tract appear to play an important role in giving a definite direction to the blood flow. This fact is demonstrated by the position of the left ventricle in the cases of prevailing hypertrophy of the left ventricular outflow tract.[7]

The Posterolateral or Ventricular Leaflet.—The smaller ventricular leaflet is not as important as the aortic leaflet, but by no means should it be disregarded in the mechanism of valve closure. This is confirmed by experimental and clinical facts. The posterolateral cusp is roughly equal to one-third of all the valvular tissue surface area. Its breadth at the line of insertion is only a few millimeters less than that of the aortic leaflet, while its height is almost one-half that of the anteromedial cusp (Table I). The contour is usually quadrangular with sloping sides and its free edge is often notched. However, the notching is seldom deep enough to be mistaken as a cleft separating the posterolateral leaflet from an additional cusp. The importance of the ventricular leaflet in the closure of the normal mitral valve seems to have been generally underestimated.

It was originally Marc Sée, a French physiologist, who, in 1875, thought that the complex mechanism of the normal mitral valve function could be simply described as an unpretentious or moderate systolic and diastolic swinging movement of the septal leaflet.[8] According to Sée, the contraction of papillary muscles would cause the anteromedial leaflet to act like a "curtain stretching obliquely from the right half of the mitral ring and across the orifice, which would remain entirely hidden." At the same time, the posterolateral ventricular wall "would march" toward the septal leaflet and come into contact with its free margin. In diastole, the aortic leaflet would swing back opening the valve. Consequently, the ventricular leaflet appeared to be a worthless structure as

far as the mechanism of the mitral valve closure was concerned. The perivalvular space was thought to be entirely obliterated in systole by the posterior ventricular wall moving toward the aortic cusp.

This old and forgotten theory has recently been revived by Harken and co-workers,[4, 5] and Gorlin and Dexter,[9] with the additional notion by Harken that "the posterior leaflet is squeezed and buttressed by the posterolateral wall of the left ventricle in systole (Fig. 3). In diastole, the myocardium swings

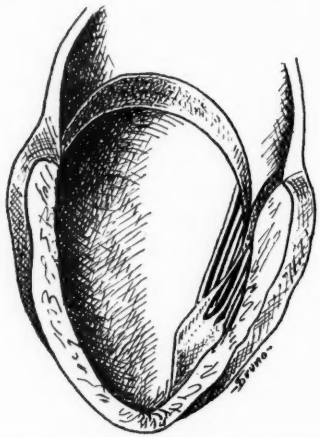


Fig. 3.—Closure of normal mitral valve according to the theory of Marc Sée, revived by Harken. The anteromedial leaflet acts like a "curtain" stretching across the orifice, which remains entirely hidden. The posterior ventricular wall moves in and buttresses the posterolateral leaflet.

away from the normal veil-like posterior mitral leaflet." Brock[10] has also admitted that this mechanism of closure may well happen sometimes. It was on account of this view that Harken[4] operated upon his first patient with unsatisfactory results.

We have tried to evaluate the anatomic and functional importance of the ventricular leaflet with experimental, morphologic, and clinical observations. From our investigation, it would appear that the theory of Sée and Harken can hardly be supported.

In the first place, the digital exploration of a normal human mitral valve by one of us (M. A. C.), in a mistaken preoperative diagnosis of mitral stenosis, revealed a remarkable billowing effect of the ventricular leaflet toward the left atrium. This had been felt in the horse's heart many years ago by the French physiologist Chauveau, who spoke of "dôme multiconcave."[11] The ventricular leaflet could be forced out into the atrium only by the blast of blood squeezed into the perivalvular space, like the wind fills out a sail. The same could not be produced by the ventricular wall being pushed against and buttressing the posterolateral leaflet. Moreover, the digital pressure on the ballooned-out ventricular leaflet produces a feeling of resilience like that of squeezing a fluid-filled bag which would hardly be felt were the muscular wall responsible

for the bulging. In addition, this same maneuver causes an immediate mitral reflux, which further suggests that the perivalvular space is not obliterated in systole.

Second, the chordae tendineae of third order, which constantly connect the ventricular leaflet with the ventricular wall, would be devoid of any importance if we were to admit that the heart wall buttresses the leaflet. As we will describe in more detail later, these chordae are there to prevent the eversion of the leaflet when the systolic thrust forcefully distends it with blood.

And third, even though the exploring finger in the heart of a dog gives one the impression of the myocardial wall supporting the ventricular leaflet, a defect in this cusp tends in no way to be closed and causes a prompt regurgitation. This would not be the case if the closure of the mitral orifice were due only to the apposition of the septal leaflet to the posterior ventricular wall. Other reasons why we cannot subscribe to the Sée and Harken theory have been discussed in previous communications.[7, 12]

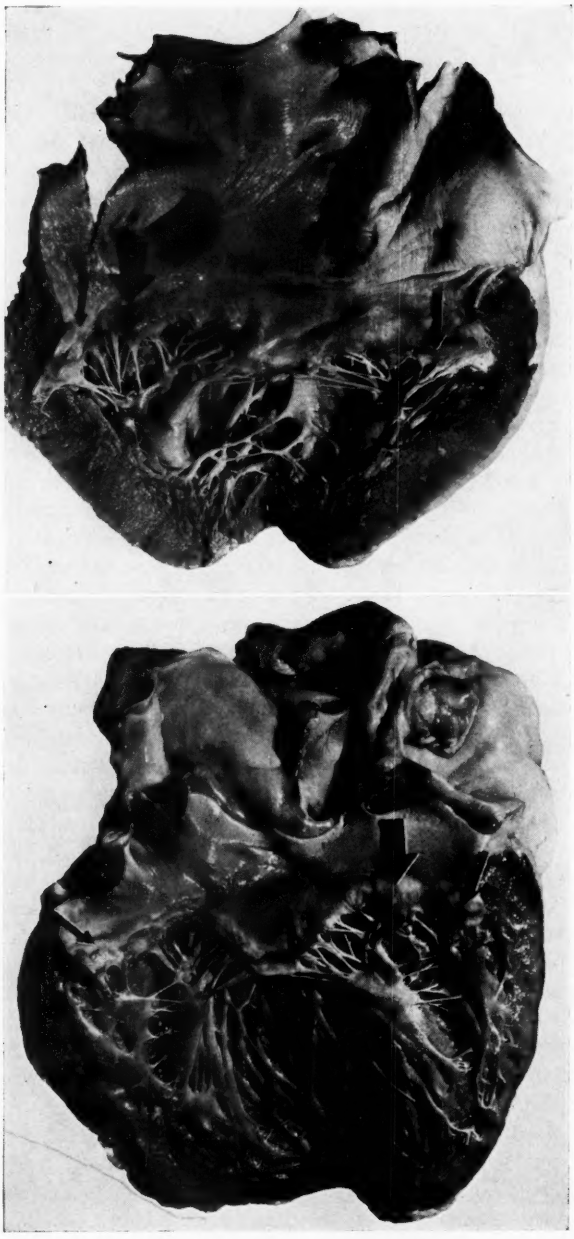
The regurgitation produced by a preponderant damage of the posterolateral leaflet is by no means of less danger to the patient, as would be the case if the above assumptions were entirely correct. The Mayo Clinic group has recently reported two peculiar cases of mitral insufficiency.[13] The first patient, a 52-year-old man, developed mitral incompetence as the result of rupture of the chordae tendineae of the ventricular leaflet and died in intractable cardiac failure one year after the episode. In the second patient, a 43-year-old rheumatic woman, a subacute bacterial endocarditis had healed producing a fusion of the posterolateral leaflet with the ventricular wall. Thirteen months later the patient died in intractable cardiac failure. These two fatal cases of mitral incompetence due to isolated involvement of the ventricular cusp indicated, by the rapidly declining clinical course, the great importance of this leaflet in the mechanism of valve closure. It should be borne in mind that Adam's patient, with a hole in the aortic cusp from a bullet, began to feel ill effects four years after the attempted suicide and lived six more years.

Junctional Tissue and Accessory Cusps.—The two major cusps are joined to each other at either extremity by a cuff of valvular tissue which we may call junctional tissue. This junctional tissue often becomes differentiated into one or two minor cusps. These are termed anterior and posterior accessory leaflets and separate the aortic from the ventricular leaflet at either extremity (Figs. 2, and 4, *A* and *B*).

Considerable controversy exists regarding the incidence of occurrence of these additional cusps as well as upon their importance from the physiologic and pathologic standpoint.

Many textbooks of anatomy claim that the two major leaflets are "ordinarily" (Testut[14]), "usually" (Quain,[15] Gray,[16] Chiarugi[17]), "some times" (Bertelli,[18] Poirier-Charpy[19]), separated at each of their extremities by the presence of small projections of valvular tissue. Many others say that the major leaflets are continuous with each other by means of a short cuff of tissue (Morris,[20] Brazier,[21] Sappey,[22] Gegenbaur,[23] Valenti[24]). However, we could not find any details as to the frequency of occurrence, importance, and size of the additional cusps or junctional tissue.

A.



B.

Fig. 4.—*A*, Human mitral valve with anterior accessory leaflet. *B*, Human mitral valve with posterior accessory leaflet. These minor cusps are indicated by two big arrows. The small arrows point to the ventricular leaflet. (Institute of Pathologic Anatomy, University of Bari Medical School, Italy, Autopsy Nos. 2595 and 2607.)

Recently in the wake of interest aroused by mitral valve surgery, two groups of workers have investigated the anatomy of the normal mitral valve. As to the occurrence of accessory cusps, the figures given by these authors are well apart from each other.

Harken and his colleagues[25] state that in 75 per cent of 35 normal hearts studied, the mitral valve pattern was that of "four triangular leaflets arranged circumferentially." That is, the presence of two major leaflets plus two additional triangular projections which they called "anterior and posterior commissural leaflets." In the remaining 25 per cent, variation was principally in the size and shape of the ventricular leaflet in relation to the two commissural leaflets. In opposite views, Rusted and associates,[3] on the basis of observations made on 100 normal hearts, state that "in 5 of the 100 hearts there were very tiny projections which conceivably could be called 'accessory cusps' at one or both commissural sites."

With the hope of presenting a contribution to the solution of this controversial matter, we studied the rate of occurrence of these additional cusps and their importance in the function of the valve as well as the importance of the junctional tissue in the cases without additional cusps.

Table III contains the data collected from our investigation. In 41 normal mitral valves (39.0 per cent), there were no accessory cusps and at their bases the major leaflets were continuous with each other by means of the so-called junctional tissue. Of the remaining 64 mitral valves with accessory leaflets, 22 had both anterior and posterior accessory, 30 had only the anterior, and 12 only posterior. Rusted and associates state that "frequently the posterior cusp is notched, and it is possible that other observers have considered one of these subdivisions of the posterior cusp as separating the main portion of the anterior and posterior cusps." This is a possibility to be seriously considered. In our experience, however, the posterior leaflet was seen to be notched in such a way as to be the source of confusion only three times. In these cases, the location of the false accessory leaflet left no doubt as to its relationship to the posterior leaflet. In other cases, the indentations on the free edge of the ventricular leaflet were not deep enough to produce the impression of an additional cusp.

TABLE III. THE FREQUENCY OF ACCESSORY LEAFLETS IN NORMAL MITRAL VALVE (105 HEARTS)

	CASES	PER CENT
Mitral valve with anterior and posterior accessory leaflets	22	20.9
Mitral valve with anterior accessory leaflet	30	28.6
Mitral valve with posterior accessory leaflet	12	11.5
Mitral valve without accessory leaflets	41	39.0
Total	105	100.0

Fig. 5 shows three normal mitral valves carefully removed from their attachments to the atrioventricular annulus and to the chordae tendineae. The heart has been opened from the posterior aspect of the left ventricle and therefore the ventricular leaflet has been divided in two portions located at either extremity of the valve. The drawing was obtained by passing a tracer around the boundary line of the valvular tissue placed over a piece of cardboard. The

greatest care was taken in preserving the same dimensions found on the valve in the opened heart. The valve *A* has four cusps, the valve *B* has three cusps, the valve *C* has only two major leaflets. From the drawing it can be concluded that the posterior junctional zone is considerably smaller than the anterior, whether or not it is differentiated into an accessory cusp.

From Table III it can be seen that an accessory leaflet was at the anterior junction zone in 50 per cent or 52 cases, while in the posterior half of the valve an additional cusp was found in 32 per cent or 34 cases. This would indicate that an accessory leaflet is absent in more than two-thirds of individuals at the posterior junctional zone. The data obtained by planimetric integration of the anterior and posterior accessory cusps (Table II) show that the posterior minor

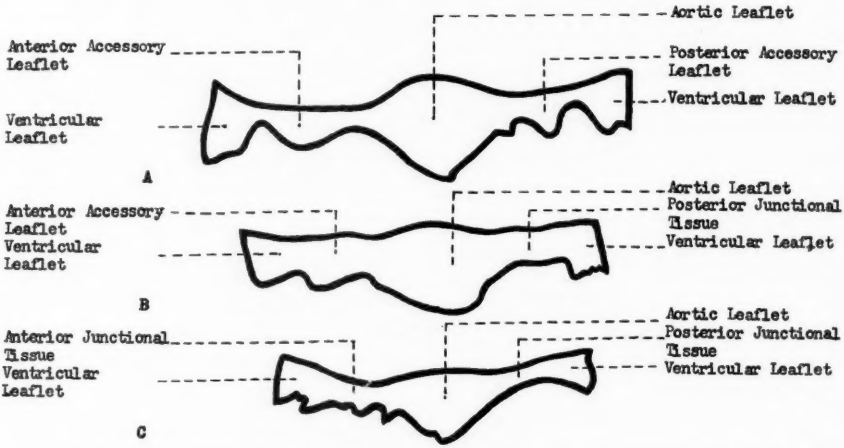


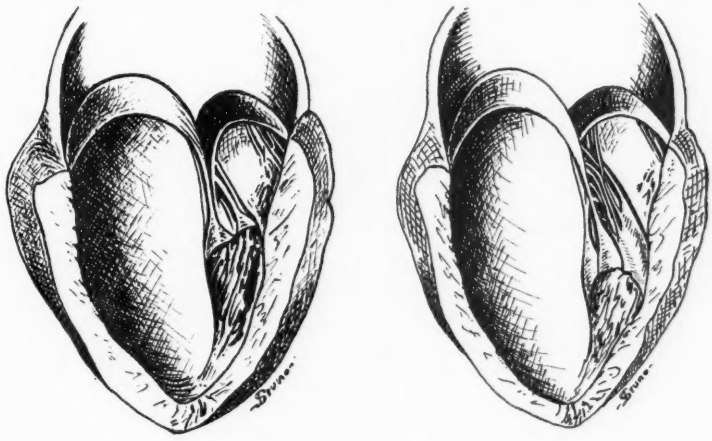
Fig. 5.—Mitral tissue of three normal mitral valves. *A*, Mitral valve with four leaflets. *B*, Mitral valve with two major leaflets and the anterior accessory cusp. *C*, Mitral valve with two major leaflets and no accessory cusps. The posterior junctional tissue is considerably smaller than the anterior, whether or not it is differentiated in an accessory cusp. (From Chiechi and Bailey: La Valvola Mitrale, Courtesy "Il Pensiero Scientifico, Editore," Rome, Italy, 1954.)

cusp surface area is consistently smaller than that of the corresponding anterior minor cusp area. When the latter is absent, the posterior minor cusp is even smaller than the anterior junctional tissue. In addition, the linear measurements listed in Table I reveal that the height and the breadth of the minor anterior leaflet are always greater than those of the posterior minor cusp. The same findings are obtained by investigating the surface area of the junctional tissue. Here again, the posterior junctional tissue was found to be consistently smaller than the corresponding anterior (Table II). From these premises it would seem logical to conclude that the posterior junctional zone is the weakest point of the mitral valve from the functional standpoint.

This can easily be proved in a normally beating human heart during a ventricular contraction. By inserting the index finger at the level of the posterior extremity of the line of closure a powerful regurgitant jet is promptly obtained. The identical maneuver anteriorly does not produce the same prompt result. The wealth of valvular tissue permits a greater degree of mutual

surface contact of the leaflets at the anterior extremity of the valve orifice (Fig. 6, *A* and *B*). The valve closure is more solid and valvular incompetence is less readily produced. On the contrary, the relative shortage of the valvular tissue at the posterior junctional zone brings about a lesser degree of surface contact of the leaflets. The valve closure, competent under normal conditions, is made promptly incompetent by the simple maneuver we have described.

This peculiar anatomic situation may have a bearing upon the observed preponderance of the localization of rheumatic valvular incompetence at the posterior portion of the mitral orifice. The healing fibrosis, consequent to a



A. *B.*

Fig. 6.—*A*, Section of normal mitral valve through the anterior papillary muscle during ventricular systole. There is a great degree of mutual surface contact near the anterior extremity of the line of closure. *B*, Same section through the posterior papillary muscle showing a lesser degree of surface contact near the posterior extremity of the line of closure. (From Chiechi and Bailey: La Valvola Mitrale, Courtesy "Il Pensiero Scientifico, Editore," Rome, Italy, 1954.)

rheumatic valvulitis, could easily destroy the few millimeters of depth of the posterior junctional tissue. This would be more so if the rheumatic process was predominantly in this region. The production of a commissure would not take place, because the intervening defect would make impossible the fusion by adhesions of the opposite leaflets at this level.[7, 12]

The function fulfilled by the junctional tissue and/or the minor accessory cusps in the normal mitral valve is that of supplying valvular tissue at either extremity of the major valve leaflets. The peculiar configuration of the major cusps with their sloping side requires the presence of additional valve tissue in order to attain a taut valvular closure at each extremity of the line of closure. It should be borne in mind that the closure of the normal mitral orifice is brought about not merely by an edge-to-edge contact of the valve cusps, but by a considerable degree of mutual contact along strips of the atrial surface of the leaflets. The latter process would not be possible without the additional valvular tissue of the junctional zone. This can easily be proved by a modified Luciani test: If in a normal heart, the left atrial wall is removed, the aorta

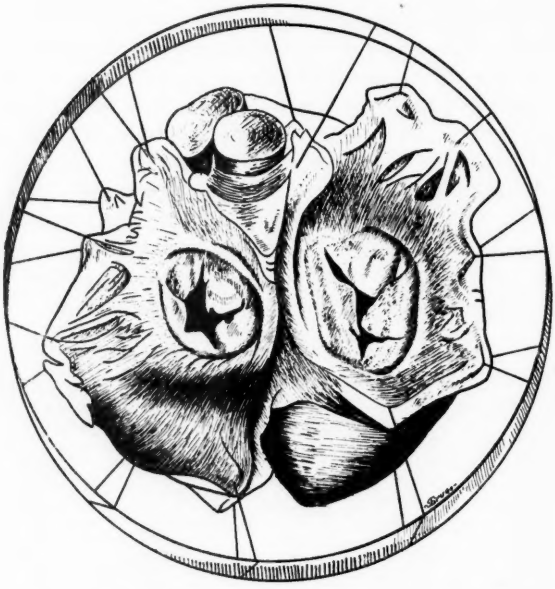


Fig. 7.—The mitral leaflets are floating on the water surface. The ventricular cavity is almost filled with water. The divided atrial walls are fixed with sutures to a circular support. The aorta and pulmonary artery openings are obstructed with corks.

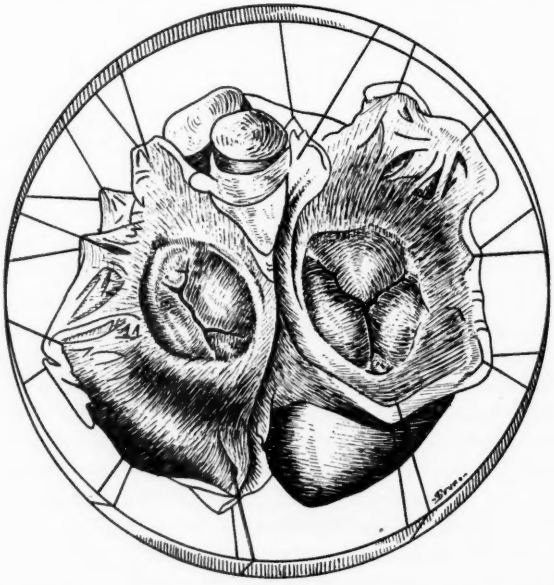


Fig. 8.—Complete closure of the mitral valve when the ventricular cavity is filled with a forceful jet of water (Luciani test). The specimen used in this experiment had a mitral valve with four cusps.

obstructed with a big cork and the ventricular cavity is almost filled with water, the valvular cusps are seen to float on the surface in the position of incomplete closure (Fig. 7). A sudden and forceful jet of a few cubic centimeters of water in the direction of the longitudinal axis of the ventricle brings about for a moment the complete closure of the valve orifice (Luciani test)[26] (Fig. 8). When the junctional zones are removed, even though the remaining valve cusps float on the surface, the further forceful introduction of water is almost without any effect (Fig. 9). The removal of the junctional zones makes impossible the

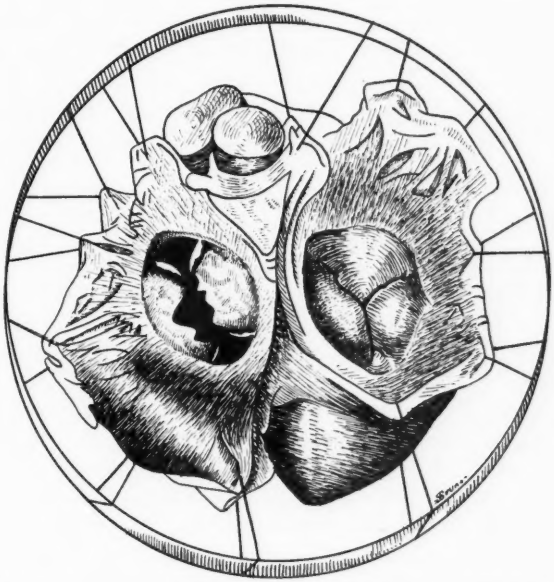


Fig. 9.—The accessory cusps have been removed. The water pours out of the ventricular cavity through the defects and the major valve leaflets never come into contact with each other.

formation of the centrifugal eddy currents to which the temporary valve closure is due. Consequently, the water pours out of the cavity through the defect at both extremities of the line of closure. The procedure is likewise unsuccessful when the junctional zone of a dead heart is cut only radially, from its free edge to the valve ring. The two divided portions never come into contact thus permitting the escape of water through the dividing lines. The last procedure can be easily performed on the living heart of a dog. Here again, the result is valvular incompetence of a moderate degree. One of us (M. A. C.) has repeatedly created valvular incompetence in the experimental animal using the original Bailey hook knife. The degree of this incompetence has unfortunately not been recorded.

Because of the importance of the junctional tissue in the mechanism of valve closure as just described, we are of the opinion that the commissurotomy, whether by separating the commissures with the finger or by cutting them apart

with a knife, should never reach the mitral ring. The opening obtained by arresting the procedure a few millimeters from the mitral annulus is usually satisfactory. By enlarging it up to the atrioventricular ring, the patient is exposed to the danger of valvular incompetence which is generally serious in a heart with mitral stenosis and a limited myocardial reserve. We have seen the production of a regurgitant jet many times following the last stroke of the finger or the knife, especially while working on the posteromedial commissure.

The last discussion brings up the still unsolved matter of the commissures in a normal heart. We believe that in the normal mitral valve there are no commissures. The textbooks of anatomy and the current medical knowledge are consistent in teaching that the mitral valve is a structure made up by two leaflets and two commissures at either extremity. Recently Rusted and coworkers[3] insisted upon the matter and, in agreement with the classical teaching, have designated as the commissures of a normal mitral valve, the normally existing junctional tissue.

Lending support to this view, it would be interesting to know where the commissures should be located in those cases with one or both accessory cusps and no junctional tissue. Moreover, close observation of a normal mitral valve, from the atrial and ventricular aspect, reveals a continuous veil of valvular tissue inserting around the circumference of the mitral orifice without any trace of commissure in the Latin sense of this word. The Latin "commissura" means joint or juncture. A joint requires connective tissue in various degrees of organization. In the case of a normal mitral valve, the junctional tissue is anatomically and histologically not different from the rest of the valvular tissue. On the other hand, when a rheumatic infection has taken place in the valve, the fibrous tissue reaction leads to the fusion of the opposite cusps and produces a commissure. For these reasons, it is difficult for us to justify the validity of the classical view. Consequently, the commissure ought to be considered as a phenomenon, uniquely and exquisitely pathologic.

Chordae Tendineae.—The atrial aspect of the normal mitral valve is a smooth, glistening surface which makes up the floor of the left atrium during ventricle systole. The ventricular aspect instead is somewhat irregular, because of the insertion of the chordae tendineae.

The chordae tendineae are tendinous, stringlike structures connecting the valvular tissue to the papillary muscles or to the ventricular myocardium. The former, distinct in chordae of first and second order, according to the accepted terminology, could be considered the tendons of insertion of the corresponding papillary muscle; the latter, chordae of third order, are shorter bands that directly connect the valve, mostly the ventricular cusp, to the ventricular wall.

From each papillary muscle the chordae tendineae spread out like the sticks of a fan to the corresponding halves of both major valve leaflets and to the junctional tissue and/or to the accessory leaflets in between. Taken together, the valve and the two fanlike arrangements of chordae could be likened to a parachute. Only occasionally has there been found a very thick chorda connecting the anterolateral muscle directly with the mitral ring.

The chordal attachment does not include the atrial aspect of the leaflets. The central portion of both major valve leaflets and the ventricular aspect of the aortic leaflet are likewise devoid of chordae.

The chordae tendineae of first order are inserted on the free edge of the leaflets. They are tenuous, threadlike structures, usually smaller and thinner and more numerous than the chordae of second order. They are frequently branched and connected with adjacent chordae by delicate anastomosis. Often they insert on the free margin of the cusp by a process of dichotomy and the two resulting branches are held together by a very thin membranous expansion of valvular tissue.

The function of these marginal chordae is that of preventing the eversion of the free margin of the leaflet into the cavity of the left atrium during ventricular systole.

The chordae tendineae of second order are thicker and are inserted on the ventricular aspect of the cusp at a short distance 0.3 to 0.6 cm. from the free edge. They end at almost regular intervals in endocardial folds but often run through the substance of the valve up to the atrioventricular ring as mentioned earlier.

In 71 per cent of the normal hearts studied in this series, it has been possible to observe chordae tendineae of second order, slightly thicker than the other, arising from the very top of the papillary muscles and inserting at each extremity of the central portion of the aortic cusp. An analogous pattern is lacking on the ventricular leaflet.

It is usually taught that these chordae going from the papillary muscles to the central portion of the anteromedial leaflet are very important in maintaining the competency of the mitral valve. Brock has even offered a pathogenetic theory of mitral stenosis, very debatable indeed,[7] based on the importance of the primary attachment of chordae tendineae that he calls "critical areas of tendon insertion."[10]

It seems to us that the functional meaning of those chordae inserting at the central portion of the aortic leaflet is that of holding steadily and firmly the cusp during ventricular systole. In addition to that, they have the task of limiting the amount of ballooning of the leaflet toward the atrium. The enormous intraventricular systolic pressures, which tend to invert the cusp into the atrium, are efficiently offset by these tendons with great tensile strength. It is well to remember that the aortic leaflet is the largest mitral cusp and yet, it has no chordae tendineae of third order. The function of these last fibrous bands seems to be essentially that of anchoring the cusp and preventing its inversion into the atrium during the ventricular contraction. It would be difficult to explain differently the immediate purpose of these short, broad tendons, stretching across the perivalvular space and joining directly the valvular tissue with the ventricular wall.

The insertion of the chordae tendineae of third order concerns mostly the ventricular leaflet, because the junctional tissue and the accessory leaflets are directly connected to the ventricular wall only rarely. This, we believe, should be the reason why the aortic leaflet has thicker chordae tendineae going from the top of the papillary muscles to its central portion, while the ventricular

cusp does not. The amount of pressure which the aortic leaflet must sustain during ventricular contraction is greater than that of the ventricular cusp. In spite of the fact that the pressure is evenly divided on every square unit of the ventricular cavity, the aortic cusp, being larger than the ventricular, has to support a greater proportion of strain.

Papillary Muscles.—The papillary muscles are the last components of the mitral valve apparatus. They belong to the system of columnae carneae of the heart and are the only cases of columnae carneae of first order. They originate from the ventricular wall and lie between the major mitral leaflets directly inferior to the valve junctional zone. Their location is anterolateral and posteromedial in the inflow tract of the left ventricular cavity. At their base the muscles are joined by columnae carneae of second and third order whose contraction brings the two muscles close together in systole.

Each chordal fan originates mainly from the apex of each papillary muscle and extends to the corresponding halves of the mitral major leaflets.

The papillary muscles may be single, double, triple, or even formed by more than three muscles. The results of our investigation on this anatomic aspect of the papillary muscles are not too different from those of Rusted and colleagues (Table IV). The muscle with an apex, only slightly or not at all grooved, was considered single. Two muscles or a muscle with two heads was considered double. Three muscles or a trifid muscle was considered triple.

TABLE IV. TYPES OF PAPILLARY MUSCLES IN 105 NORMAL HEARTS

TYPES OF PAPILLARY MUSCLES	ANTEROLATERAL MUSCLES		POSTEROMEDIAL MUSCLES	
	CASES	PER CENT	CASES	PER CENT
Single	87	82.8	31	29.5
Double	15	14.3	57	54.3
Triple	3	2.9	12	11.4
More than three	–	–	5	4.8

More than four-fifths of the anterolateral papillary muscles proved to be single, while more than two-thirds of the posteromedial muscles were multiple. As pointed out by Rusted the most frequent combination was that of a single anterolateral muscle with a double or triple posteromedial papillary muscle, occurring in our series in almost two-thirds of the cases. Occasionally, the accessory cusps have their chordal attachments on an independent small muscle head at the anterolateral and posteromedial sites.

Another aspect of the anatomy of papillary muscles which has been investigated is that of the possibility of their becoming interlocked into one another during ventricular systole. The old anatomists thought that in systole the usually single and round-shaped anterolateral muscle could approximate and occupy the hollow formed by the usually multiple posteromedial muscle. It was entertained also that the posteromedial muscle was placed in such a way on the posteromedial wall of the heart as to offer a hollow surface to the anterolateral muscle. This nice and elegant view, on which Lutembacher has also written,[27] would not be given support by our work. Table V lists the data on the inner surface of the papillary muscles; that is, the surface facing the

TABLE V. TYPES OF INNER SURFACE OF PAPILLARY MUSCLES IN 105 NORMAL HEARTS

TYPES OF PAPILLARY MUSCLES	ANTEROLATERAL MUSCLES				POSTEROMEDIAL MUSCLES			
	CONVEX		CONCAVE		CONVEX		CONCAVE	
	CASES	PER CENT	CASES	PER CENT	CASES	PER CENT	CASES	PER CENT
Single	84	80.0	3	2.8	31	29.5	–	–
Double	8	7.7	7	6.8	15	14.3	41	39.0
Triple	1	0.9	2	1.8	4	3.8	14	13.4

long axis of the left ventricle. It can be seen that in 50 of 105 normal hearts, the inner surface of the posteromedial muscle was convex instead of being concave as would have been the case if the above-mentioned view was entirely correct. It can be reasonably expected, however, that the muscles come into mutual contact in systole, even though their arrangement does not appear to be set for an interlocking contact in the sense that the early anatomist described.

CLOSURE OF THE NORMAL MITRAL VALVE

Considering the valvular tissue surface area as a whole in relation to the mitral orifice area, it is of interest to observe that the former, by and large, exceeds the latter. The relationship between the two areas is, according to our investigation, very close to 2 to 1 in many cases. In a few cases the relation is 1.5 to 2, but never is it less than that. In other words, there is always an excess of valvular tissue in relation to the area of the orifice. The difference becomes even greater in systole because of the sphincterlike action of the atrioventricular ring which further reduces the orifice's area. The closure of the mitral aperture is therefore the tautest possible, because the valve leaflets not only meet at their free margins, but they come into very extensive mutual contact along most of their atrial surface.

We can visualize well the mechanism of closure of the normal mitral orifice by the valve leaflets as a process involving three succeeding phases. At first, the leaflets meet edge to edge; then, under the progressive contraction of the myocardial fibers and the increased intraventricular pressure, the chordae tendineae are pulled while the cusps come into surface contact, ballooning toward the atrial cavity; in the last phase, the mutual surface contact between the leaflets becomes more and more extensive, so that when the blood is forced out into the arota by the contraction of the deep circular muscles of the heart, the leaflets are disposed against each other in an almost vertical position (Luciani).

The mechanism of valve closure, far from being so simple, is the result of complex interaction of the various components of the valve apparatus and the ventricular and atrial myocardium.

Hydrodynamic pressure changes following the rapid inflow and atrial systole would be entirely responsible for the first phase according to some authors (Henderson and Johnson,[28] Little[29, 30]). A modern version of this view is that bringing into play the Venturi effect at the time of rapid inflow when the valve is in the condition of incomplete closure (Rodbard[31]). Still some others believe that the production of turbulent flow and the consequent formation of eddies behind the cusps at the end of the atrial systole could drive the

mitral leaflets one against the other (Luciani). There are investigators, however, who are of the opinion that the valve closure by atrial mechanism is incomplete and temporary (Dean,[32] Wiggers,[33] Smith and co-workers[2]).

The second phase of the mitral valve closure is simultaneous with the ventricular systole. The contraction of the superficial layers of myocardial fibers together with that of papillary muscles causes various events to take place. The atrioventricular ring reduces somewhat its circumference, the intraventricular pressure rises rapidly, causing a forceful pull of the chordae tendineae and the bulging of the valvular tissue toward the atrium. The mitral leaflets from the marginal contact of the first phase progress to a surface contact over a considerable portion of their atrial aspect at the end of this phase.

When the intraventricular pressure exceeds the aortic pressure at the onset of the maximum ejection period, the valve closure is made perfectly hermetic. The contraction of the deep sinospiral muscle, embracing both ventricles at their base, and that of the deep bulbospiral muscle, encircling the mitral and the aortic orifice,[34] further decrease the circumference of the atrioventricular annulus. While the blood is being expelled into the aorta by the contraction of these muscles, the mitral leaflets come into mutual surface contact over almost all of their atrial aspect and may even reach a vertical position. The mitral orifice is brought down to a fraction of its original area by the constricting action of the deep circular muscles and the redundant valvular tissue is pulled down vertically. This goes on for the maximum and reduced ejection periods up to the onset of diastole. With the opening of the mitral valve, the rapid inflow of blood sets the leaflets in a position of incomplete closure and the cycle starts all over again.

SUMMARY AND CONCLUSIONS

The purpose of our investigation was to study some of the features of the normal mitral valve, which have received only scant attention in the voluminous literature connected with mitral valve disease. It was also our concern to assess the importance of these structures in the mechanism of mitral valve closure. The mitral valve apparatus was described in toto in order to present a clear outline of its functional anatomy.

We found some widely accepted notions about functional anatomy of the mitral valve, which have not received support from our research. No anatomic or functional basis was found for the alleged baffling action of the aortic cusp. Neither was it possible to accept the theory that the mitral valve is closed by the sole action of the aortic leaflet, while the posterior wall of the heart buttresses the posteromedial leaflet.

We believe that the importance of the ventricular leaflet in the mechanism of the valve closure is strictly proportional to the extent of its surface area as compared with that of the other portions of the mitral veil. If the ventricular cusp is to serve no useful purpose in the mechanism of valve closure, there would be no reason for it to be there. Furthermore, the notion that valvular incompetence with the opening at the outflow tract of the left ventricle is more

serious than valvular incompetence due to isolated involvement of the ventricular leaflet, remains open to question. The seriousness of a regurgitant lesion is governed mainly by the sectional area of the defect and much less by its spatial orientation. The 2 cases from the Mayo Clinic, mentioned earlier, show convincingly the extreme gravity of a regurgitant lesion of the ventricular leaflet. It is true that compensatory mechanisms may occur posteriorly, but these do not appear to be related to the posterior ventricular wall.

A constituent of the mitral valve which needs to be better understood is the junctional tissue. It is frequently designated as a valvular commissure, but we have described the reasons for not accepting the term "commissure" when speaking of the junctional tissue in a normal mitral valve.

In the diseased mitral valve, the commissures have the same location as the junctional zones in a normal mitral valve. However, these junctional structures make up only the deepest part of the commissures, i.e., the part closest to the mitral ring.

Undoubtedly, the junctional zones are of considerable importance from the anatomic as well as the physiologic standpoint. As recently as 1924, Coombs[35] theorized that the progressive shrinkage of the junctional tissue from rheumatic involvement was responsible for the production of mitral stenosis.

Our study of the junctional zone in the normal mitral valve revealed that (1) the junctional tissue more often than not is differentiated in one or two minor cusps, succeeding in alternation to the major leaflets, (2) an accessory cusp is lacking more often posteriorly than anteriorly, (3) the amount of valvular tissue is smaller posteriorly than anteriorly, and (4) the junctional zone is essential to good function of the valve because its division, in the experimental animal, causes a moderate degree of valvular incompetence.

As a corollary to these findings, it follows that the posterior portion of the mitral valve is the least gifted with valvular tissue and therefore the weakest part of the valve. We believe that the observed preponderance of valvular incompetence at the region of the posterior commissure is probably due to this shortage of valvular tissue in this region. The posterior junctional tissue could be destroyed by a rheumatic process more easily than the anterior which is richer in valvular tissue. We are of the opinion that no commissurotomy should ever reach the mitral ring, because of the importance of maintaining a cuff of valvular tissue to insure closure of the orifice. By splitting the valvular tissue up to the annulus, a fatal regurgitation might be produced. It is well known that a posterior commissurotomy more often is followed by a surgically produced valvular incompetence than is an anterior separation. If the operation has been adequate, that is, if the division has been in the line of the commissure, the production of incompetence could be explained only by the fact that the junctional tissue has been divided along with the commissure. This is much more easily done posteriorly because the posterior commissure is usually less deep than the anterior and the atrioventricular annulus is reached promptly by a stroke of the finger or of the knife.

Grateful acknowledgment is hereby accorded to Professor Italo Rizzi, Director of the Institute of Pathologic Anatomy, University of Bari Medical School, Italy, for the courtesy of making available autopsy material.

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PROLONGATION OF SAFE PERIOD OF VENOUS INFLOW OCCLUSION IN HYPOTHERMIC STATE BY CORONARY AND CAROTID ARTERY PERFUSION WITH OXYGENATED BLOOD

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HELPFUL as hypothermia has been as an aid for open cardiac surgery, it has two principal disadvantages. The first is concerned with increased myocardial irritability and particularly with the hazard of ventricular fibrillation. In other studies,[1-6] we have demonstrated that this danger can be minimized by anesthetic infiltration of the superior vena caval-right atrial junction, by operative sympathetic denervation of the heart or sympathetic blockade with drugs and, as Montgomery and associates have also demonstrated,[7] by stimulation of the right vagus nerve. Other workers have confirmed the effectiveness of anesthetic block of the vena caval-right atrial junction.[8-10] The other disadvantage relates to the relatively brief period of venous inflow occlusion compatible with recovery without neurologic damage. This study is concerned with this problem. It deals with the effect of perfusing, with oxygenated blood, the coronary and carotid arteries.

MATERIAL AND METHODS

Healthy mongrel dogs weighing between 6 and 13 Kg. were used. They were anesthetized by the intravenous administration of from 2 to 4 c.c. of 10 per cent thiopental sodium, intubated and hyperventilated with 100 per cent oxygen by means of an intermittent insufflation apparatus producing between 35 and 45 respirations per minute. The animals were cooled to a temperature of 30° C. by immersion in a bath of water and crushed ice. If shivering occurred, it was controlled by administering, temporarily, a mixture of ether and oxygen. The animals were then removed from the ice bath and by the time the chest was entered the temperature had fallen an additional 3° to 5° C.

The blood for infusion was obtained by bleeding hyperoxygenated normal dogs from the femoral artery. The blood was collected in vacuum bottles containing either 20 mg. of heparin or a small amount of sodium citrate, citric acid, and dextrose. The blood was withdrawn just before each experiment and was stored, temporarily, in a refrigerator kept at 4° C., for twenty or thirty minutes. The blood was grossly well oxygenated. In some of the experiments, this arterialized blood was saturated further by bubbling through it a jet of 100 per cent oxygen.

In each case, the right-atrial superior vena caval junction was infiltrated with 1 per cent procaine solution until satisfactory slowing of the heart occurred and the charac-

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Aided by grants from the National Heart Institute, the United States Public Health Service, the Frederick M. Douglass Foundation, the James W. Riley Memorial Association, and the Indiana Heart Foundation.
Received for publication March 2, 1956.

teristic disappearance of, or reduction in voltage of, the electrocardiographic P wave. The injection was repeated every fifteen minutes when heparinized blood was used. It was repeated just prior to release of vena caval clamps when citrated blood was employed.

The venae cavae were occluded with Pott's clamps and one minute later the aorta was cross-clamped distal to the point of entry of the perfusion catheter. Immediately after the perfusion was begun, a 4 to 5 cm. right ventriculotomy incision was made. The animal was placed in Trendelenburg position. The right ventricle was kept empty of blood by aspiration. From twenty to thirty minutes later, the ventriculotomy was repaired with a continuous suture of silk. The superior vena caval clamp was then released and two or three minutes later, the inferior vena caval clamp.

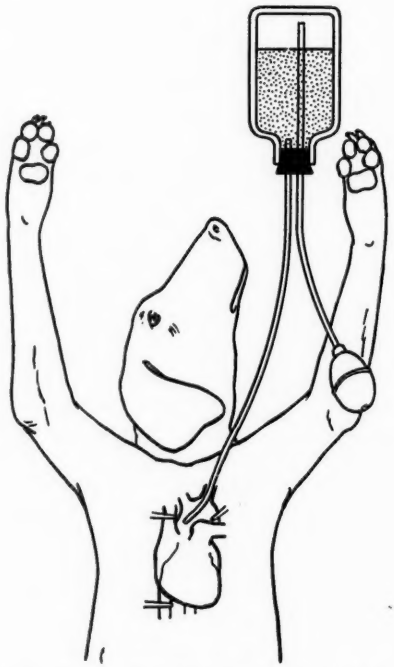

Fig. 1.—Drawing illustrating type of perfusion. Oxygenated blood is delivered from a transfusion bottle suspended over heart, the rate of flow being regulated by manometrically controlled pressure within the flask.

During the perfusion, all blood lost was recovered by aspiration and measured carefully. Intermittently, in cases of carotid and coronary perfusion, blood was allowed to escape through the opened heart while the superior vena caval clamp was momentarily released in order to equalize the amount of blood perfused and that recovered by aspiration.

The oxygenated blood was perfused at a rate of from 25 to 35 c.c. per minute, by gravity flow, using manometrically controlled pressure in the infusion bottle to regulate the speed of administration (Fig. 1). At the completion of the experiment, the perfusion catheter was removed. The stab wound in the aorta was closed with silk sutures, or the left subclavian artery was ligated. The pericardium was approximated loosely. The chest wound was repaired. Catheters were left in the pleural cavity until rewarming had occurred. As soon as the chest wall was repaired, the animal was warmed to a temperature of approximately 36° C. by immersion in a water bath kept at 45° C. The indwelling catheters were

then removed after aspiration was carried out. The animal was left in a warm room for the next sixteen to eighteen hours. Two hundred thousand units of penicillin were administered daily for the first three or four days.

In those experiments in which citrated blood was used for perfusion and the heart was in standstill, cardiac massage was instituted after release of the vena caval clamps. Five cubic centimeters of a 20 per cent solution of calcium gluconate was injected into the right ventricle either before or one minute after institution of cardiac massage. When heparinized blood was used and cardiac contractions were maintained, no calcium was administered and massage was not carried out. At the completion of the experiment, protamine was given, 1.5 mg. for each milligram of heparin perfused.

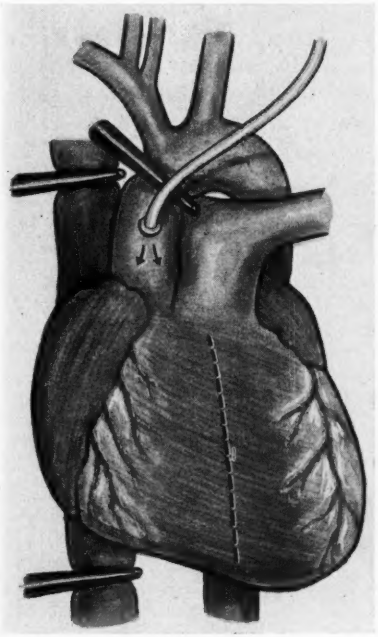

Fig. 2.

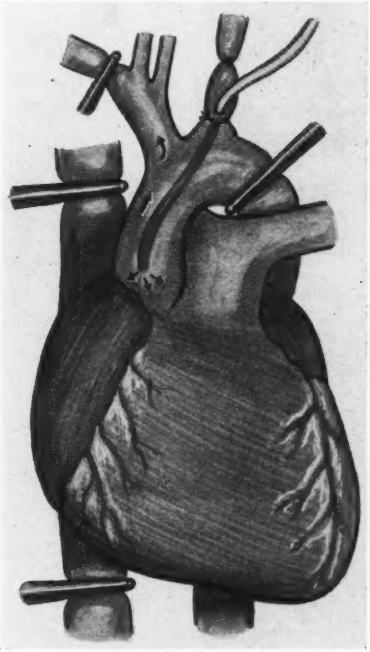

Fig. 3.

Fig. 2.—Drawing illustrating perfusion of coronary arteries during venous inflow occlusion.

Fig. 3.—Drawing illustrating perfusion of coronary and carotid arteries during venous inflow occlusion.

Whenever ventricular fibrillation occurred in animals having received either citrated or heparinized blood, vigorous cardiac massage was begun immediately. Unless fibrillation disappeared and sinus rhythm returned, massage was continued until the heart was of good color and the fibrillation strong. In almost all cases, 1 c.c. of 1 to 10,000 epinephrine solution was administered into the right ventricle in order to strengthen the myocardial tone. Three successive electric shocks of 170 volts and 1/10 of a second duration were then applied.

Two groups of experiments were carried out. In the first, the coronary arteries alone were perfused. In these animals, the chest was entered through a right anterolateral fourth intercostal space incision. A small polyethylene catheter with a flange on its end was introduced into the ascending aorta through a small stab wound made in a portion of the aortic

wall temporarily excluded from the lumen by application of a curved Pott's ductus clamp. Once the catheter was in place, the clamp was removed and the catheter secured to the aortic wall by two purse-string sutures of No. 5-0 arterial silk. When the perfusion was begun, the aorta was clamped distal to the point of entry of the catheter and proximal to the site of origin of the brachiocephalic trunk (Fig. 2).

In the second group, either a sternal-splitting incision or a bilateral anterior thoracotomy with sternal transection was used. The perfusion catheter was introduced into the ascending aorta through the left subclavian artery which was ligated snugly distal to the site of entry of the catheter. The right subclavian artery was occluded at the point of its origin with a rubber-shod serrefine clamp, and the aorta with a Pott's ductus clamp distal to the origin of the left subclavian artery (Fig. 3).

OBSERVATIONS

In those animals in which heparinized blood was used for perfusion, the heart continued beating with a normal rhythm during the entire period of vena caval occlusion (Fig. 4). With the passage of time, the rate tended to decrease. In general, the heart maintained good color and toward the end of the occlusion

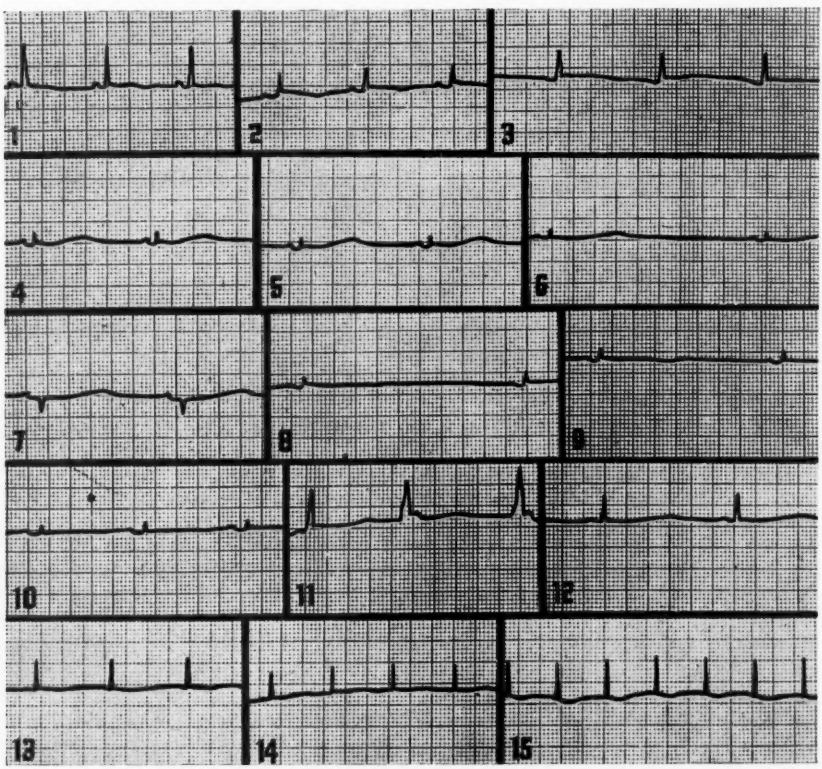

Fig. 4.—(Lead II) Electrocardiographic tracings in case of coronary and carotid artery perfusion with heparinized oxygenated blood. *1*, chest open, 26.5° C. *2*, prior to, and *3*, immediately after procaine infiltration of right atrial-superior vena caval junction. *4*, *5*, and *6*, After 5, 10, and 16 minutes of perfusion. *7*, After second procaine infiltration. *8*, After 29.5 minutes of perfusion. *9*, Following removal of superior vena caval clamp. *10*, Following removal of inferior vena caval clamp. *11*, After closure of pericardium. *12*, Immediately after repair of chest incision. *13*, *14*, and *15*, At body temperatures of 28°, 32°, and 36° C.

time, when the rhythm was slower, the heart was even pinker than it was initially. When ventricular fibrillation occurred, it always developed after termination of the perfusion and release of the vena caval clamps.

When citrated blood was used, the cardiac rate slowed progressively and standstill usually occurred within from five to eight minutes (Fig. 5). In an exceptional animal, a feeble heartbeat continued for a longer period. The heart remained pink and its color became even brighter once standstill took place.

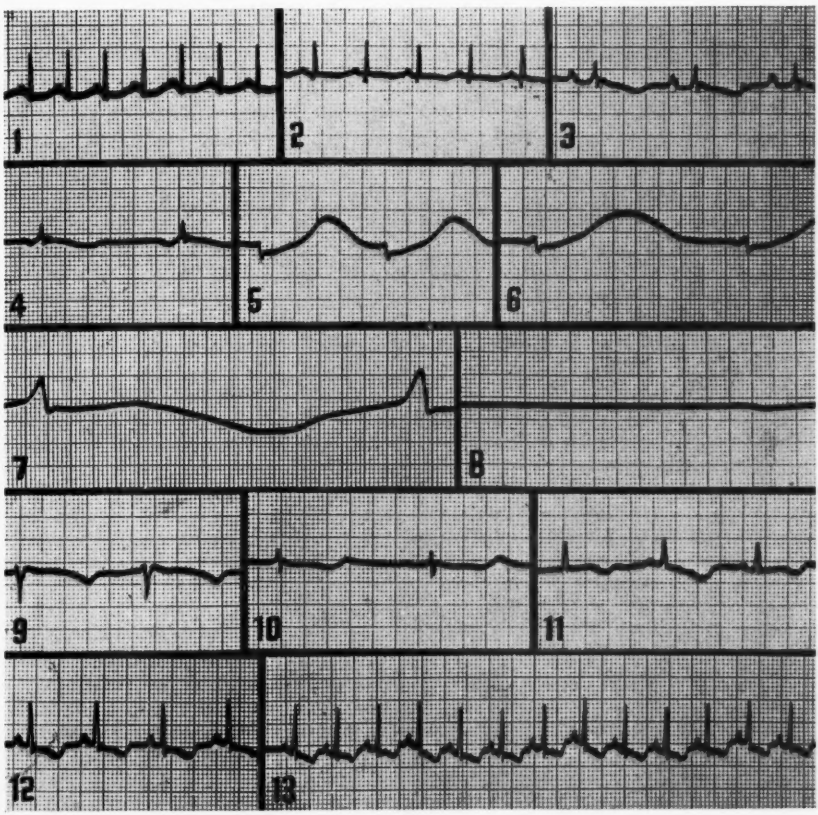

Fig. 5.—Electrocardiographic tracings (Lead II) in case of coronary and carotid artery perfusion with citrated oxygenated blood. *1*, *2*, and *3*, at body temperatures of 37°, 33°, and 26.5° C. *4*, Following procaine infiltration of right atrial-superior vena caval junction. *5*, *6*, *7*, and *8*, After 3, 5, 8, and 10 minutes of perfusion. *9*, following cardiac massage and intracardiac calcium. *10*, following closure of the pericardium. *11*, after repair of chest incision. *12* and *13*, at body temperatures of 32° and 36° C.

During this period, also, a striking observation was that the coronary sinus and the Thebesian blood became more arterial in character as the perfusion proceeded (Table I). Ventricular fibrillation occurred much more commonly when intracardiac calcium was administered after release of the vena caval occlusion and before institution of cardiac massage than when given after one minute of cardiac massage.

TABLE I. OXYGEN SATURATION OF CORONARY SINUS BLOOD DURING CORONARY AND CAROTID ARTERY PERFUSION WITH CITRATED OXYGENATED BLOOD*

NUMBER OF DOG	INTERVAL AFTER BEGINNING OF PERFUSION IN MINUTES		
	2.5	9.5	15
1	56.8	69.9	77.5
2	52.6	64.2	76.8

*The saturation of the perfused blood was 87.8 per cent in Dog 1, 86.5 per cent in Dog 2.

Animals with Coronary Artery Perfusion.—There were 13 animals in this group. In 8, heparinized blood was utilized (Table II). The temperatures of the animals ranged from 24° to 28° C. and the period of venous inflow occlusion from 25 to 28.5 minutes. The blood perfused ranged from 2.1 to 2.8 c.c. per kilogram per minute. In 2 animals, ventricular fibrillation occurred following release of the vena caval clamps and defibrillation was successfully accomplished in both. Two animals, after having made a good immediate recovery, died the day following surgery with hemothorax and hemorrhagic atelectasis. The others made a good recovery and were sacrificed in from 20 to 170 days.

TABLE II. CORONARY PERFUSION WITH HEPARINIZED BLOOD*

DOG NUMBER	WEIGHT OF DOG (KG.)	TEMPERATURE OF DOG (° C.)	TIME CAVAL OCCLUSION (MIN.)	BLOOD PERFUSED (C.C.)	VENTRICULAR FIBRILLATION	FINAL RESULT
2	10	26	25.5	510	No	Stuporous 1 day after surgery, normal afterward; sacrificed 36 days later
168	8	25.5	25	400	No	Same; sacrificed 170 days later
171	8	28	26	600	No	On his feet and well the morning after surgery; dead few hours later from hemothorax
172	6.5	27	26	350	No	Weakness hind legs for 2 days, normal afterward; sacrificed 20 days later
175	7.2	26.5	26	400	No	Stuporous 1 day, normal afterward; sacrificed 160 days later
176	6	26.5	26	360	Yes	Stuporous 1 day, normal afterward; sacrificed 40 days later
185	7.5	26.2	26	400	Yes	Stuporous 1 day; well afterward; sacrificed 155 days later
200	10	25	28.5	600	No	On his feet and well following morning; dead few hours later, hemothorax

*The perfusion rate ranged between 2.1 and 2.8 c.c. per kilogram per minute.

In 5 animals, citrated blood was used (Table III). The temperature ranged between 24° and 26° C. and the period of inflow occlusion from 27.5 to 29.5 minutes. The blood perfused varied from 2 to 2.3 c.c. per kilogram per minute. In 2 animals, intracardiac calcium was administered after release of the vena caval clamps and before cardiac massage was instituted. Ventricular fibrillation promptly developed and in both successful conversion was achieved. In the other 3, intracardiac calcium was administered after a period of cardiac massage and fibrillation did not occur.

TABLE III. CORONARY PERFUSION WITH CITRATED BLOOD*

NO. NUMBER	WEIGHT OF DOG (KG.)	TEMPERATURE OF DOG (° C.)	TIME OF CAVAL OCCLUSION (MIN.)	BLOOD PERFUSED (C.C.)	VENTRICULAR FIBRILLATION	FINAL RESULT
207	10.5	25.5	27.5	600	Yes	Weak, stuporous for 3 days, normal afterward; sacrificed 62 days later
225	11.2	26	27.5	600	Yes	In good condition day after surgery; sacrificed 61 days later
227	9.2	24	29.5	560	No	In good condition day after surgery; sacrificed 70 days later
233	9.5	26	28.5	580	No	In good condition day after surgery; sacrificed 72 days later
240	9.5	24.8	28.5	590	No	In good condition day after surgery; sacrificed 114 days later

*The perfusion rate ranged between 2 and 2.3 c.c. per kilogram and per minute.

Of the 13 animals in this group, 5 were stuporous for one day and thereafter had no evidence of neurologic damage. One additional animal was weak and stuporous for three days after which he seemed perfectly well. Still another animal showed weakness of the hind legs for two days and was normal afterward. There was no evidence of even transient neurologic damage in the re-

TABLE IV. CORONARY AND BRAIN PERFUSION WITH HEPARINIZED BLOOD*

DOG NUMBER	WEIGHT OF DOG (KG.)	TEMPERATURE OF DOG (° C.)	TIME CAVAL OCCLUSION (MIN.)	BLOOD PERFUSED (C.C.)	VENTRICULAR FIBRILLATION	FINAL RESULT
1	10.2	25.5	29	180	No	Perfectly well day after surgery, no brain damage; sacrificed 120 days later
159	8.5	27.5	29.5	900	No	Same; sacrificed 110 days later
173	7	28	29	650	No	On his feet and well following morning; dead few hours later, hemothorax and intrapulmonary bleeding
179	7.8	28	30	760	No	No brain damage; sacrificed 20 days later
182	6.4	25.5	30	550	No	No brain damage; sacrificed 19 days later
183	6.2	25.8	30	620	No	No brain damage; sacrificed 20 days later
190	12	26.5	31.5	600	No	Dead late following day, hemothorax, intrapulmonary bleeding
191	8	26.5	31.5	600	No	Same
193	9.2	25	33	750	No	No brain damage; sacrificed 90 days later
246	11	26	35	950	Yes	No brain damage; sacrificed 100 days later
250	12	25	38	950	Yes	No brain damage; sacrificed 25 days later
272	9.8	26	35	1,000	No	Dead after rewarming, hemorrhagic atelectasis
283	10.5	25	34	870	No	No brain damage; sacrificed 30 days later

*The perfusion rate ranged between 1.6 and 4.7 c.c. per kilogram per minute.

maining 6. During the period of venous inflow occlusion, the pupils became widely dilated in all animals but normal pupillary constriction returned in each as rewarming took place.

Animals With Coronary and Carotid Artery Perfusion.—There were 28 dogs in this group. Heparinized blood was used in 13 (Table IV). The temperature ranged between 25° and 28° C. and the period of inflow occlusion from 29 to 38 minutes. The blood perfusion varied between 1.6 and 4.7 c.c. per kilogram per minute. In two instances, ventricular fibrillation occurred shortly after release of the vena caval clamps. Successful conversion to sinus rhythm was accomplished in both. In 12 animals, there was prompt recovery without evident neurologic damage. In 1 case, the animal was successfully rewarmed and regained consciousness but died with hemorrhagic atelectasis a short while later. Three additional dogs, following an apparently good imme-

TABLE V. CORONARY AND BRAIN PERFUSION WITH CITRATED BLOOD*

DOG NUMBER	WEIGHT OF DOG (KG.)	TEMPERATURE OF DOG (° C.)	TIME CAVAL OCCLUSION (MIN.)	BLOOD PERFUSED (C.C.)	VENTRICULAR FIBRILLATION	FINAL RESULT
208	9.3	25.5	35	800	Yes	No brain damage; sacrificed 112 days later
211	9.2	26	38	900	Yes—arrested by simple massage	Stuporous 5 days; died; fluid in chest, probable brain damage
223	13	25.5	28	820	Yes—arrested by simple massage	No brain damage; sacrificed 45 days later
230	10.5	24.5	35	1200	No	No brain damage; sacrificed 105 days later
236	10	25.5	35	1050	No	No brain damage; sacrificed 104 days later
241	10	26	35	875	No	No brain damage; sacrificed 90 days later
244	10.2	26	34.5	840	No	No brain damage; sacrificed 60 days later
255	12	26.5	30	650	Yes	No brain damage; sacrificed 39 days later
256	11	26	34.5	850	No	No brain damage; sacrificed 35 days later
261	13	25	34.5	700	No	No brain damage; sacrificed 34 days later
271	11.4	25	35	1100	No	Death; pulmonary edema after resumption of circulation, inadequate removal perfused blood
273	10	25	39.5	900	No	No brain damage; sacrificed 20 days later, empyema
274	10.6	26	35	850	No	No brain damage; dead 3 days after surgery, almost total atelectasis of lungs
314	11	25	32	870	No	Dead late day after surgery, hemorrhagic atelectasis of lungs
333	11	25	29	600	No	No brain damage; sacrificed 78 days later

*The perfusion rate ranged between 1.5 and 3.4 c.c. per kilogram per minute.

diate recovery, died late the day after surgery with hemothorax and hemorrhagic atelectasis. The remainder were in good health until sacrificed from 19 to 120 days after operation.

Citrated blood was used in 15 animals (Table V). The temperature ranged between 24.5° and 26.5° C. and the period of inflow occlusion between 29 and 39.5 minutes. The blood perfused varied between 1.5 and 3.4 c.c. per kilogram per minute. Ventricular fibrillation developed in 3 animals in which intracardiac calcium was given after release of the vena caval clamps and before cardiac massage was begun. Only 1 animal given intracardiac calcium after one minute of cardiac massage developed ventricular fibrillation. Conversion to sinus rhythm followed cardiac massage in 2 cases and in the other 2, electric shock was successfully employed. One animal (No. 271), which through error was given 400 c.c. more blood by perfusion than was removed, developed acute pulmonary edema shortly after release of vena caval occlusion and died. The remainder recovered, though 2 animals died one and three days after operation with hemorrhagic atelectasis. One exceptional animal was stuporous for five days after operation and then expired. He had been given a perfusion of 900 c.c. of blood during a period of thirty-eight minutes, or 2.5 c.c. per kilogram per minute. There was no evidence of neurologic impairment in the remainder. In no animal perfused with oxygenated blood into coronary and carotid arteries was even transient full pupillary dilatation observed.

DISCUSSION

These experiments demonstrated that perfusion of the coronary arteries alone with oxygenated blood lengthens to from twenty-five to thirty minutes the period of venous inflow occlusion compatible with recovery. Nearly one half of the animals, however, exhibited neurologic abnormalities for a short period following operation, though they recovered and remained well. When both coronary and carotid arteries were perfused, venous inflow occlusion could be maintained for from 29 to 39.5 minutes without evidence of neurologic damage. It seems clear that perfusion of the carotid, as well as of the coronary arteries, affords protection over and beyond that conferred by coronary perfusion. The fact that great protection results from coronary perfusion alone suggests that avoidance of neurologic damage is, to some degree, dependent upon protection of the heart itself during the period of inflow occlusion and prompt recovery of good cardiac function afterward.

We have not, ourselves, determined the upper limit of safe inflow occlusion in hypothermic animals without perfusion. We and others have subjected animals under moderate hypothermia to periods of caval occlusion of fifteen minutes with recovery. Gollan and his associates[11] reached the conclusion that even at body temperatures as low as 14° C. the hypothermic animal cannot withstand interruption of cardiac function for more than twelve minutes.

Edwards and his colleagues[12] found that a ventriculotomy performed on moderately hypothermic dogs during a 10-minute period of inflow occlusion invariably resulted in ventricular fibrillation, but that a low incidence of fibrillation was noted when ventriculotomy with production and closure of a septal

defect was performed under similar circumstances but with coronary artery perfusion. Five of 7 animals survived inflow stasis for twenty minutes during perfusion of the heart, brain, and upper extremities. Shumway, Gliedman, and Lewis[13] demonstrated that coronary perfusion with either oxygenated or venous blood in moderately hypothermic dogs permitted one to occlude the venae cavae relatively safely for twenty minutes. Gaertner and his colleagues[14] have recently reported that coronary and brain perfusion extended the period of safe cardiac exclusion. In all of these experiments, the perfusion was carried out by means of a mechanical pump.

The perfusion rate in the experiments of Edwards and his associates was 10 and 20 c.c. per kilogram per minute. Shumway and his colleagues found that coronary perfusion with venous blood at a flow rate of 50 c.c. per minute was satisfactory for maintaining an acceptable degree of myocardial oxygenation. Gaertner, Kay, Isaacs, and Dever used a perfusion rate of from 80 to 120 c.c. of blood per minute.

Our experiences suggest that simple gravity flow, utilizing pressure in the infusion flask to regulate the speed, is adequate for both coronary, and carotid, and coronary perfusion. They further suggest that a rate of between 1.5 and 4.7 c.c. per kilogram per minute is adequate. Most of our animals were perfused at the rate of approximately 2.5 c.c. per kilogram per minute.

Shumway, Gliedman, and Lewis had no survivors when citrated blood was used. We have found that citrated blood can be used safely in dogs provided one massages the heart vigorously after release of the vena caval clamps, administers a small amount of calcium into the right ventricle, and uses electric shock for the occasional animal in which fibrillation develops and is not converted by massage alone.

Shumway and his associates noted troublesome bleeding when heparinized blood was used. This was also the experience of Gaertner and his colleagues who, however, had the impression that death in their animals was mostly due to pulmonary congestion. We encountered the same hemorrhagic difficulty when heparinized blood was used. In subsequent experiments,[15] this difficulty has apparently been overcome. It has been learned that delaying the perfusion for two minutes after occluding the venae cavae and maintaining respiration during this interval seemingly eliminates the hemorrhagic tendency. This plan permits the heart and lungs to be largely emptied of blood before the perfusion is started. Animals treated in this fashion have developed neither hemorrhagic atelectasis nor troublesome hemothorax.

Whether the studies reported will prove of real value in clinical cases, we do not know at this time. Judging from them, it would seem reasonable to suppose that protecting the patient by procaine blockade of the right atrial-superior vena caval junction and perfusing the coronary and carotid arteries with oxygenated blood will likely permit a relatively long period of inflow occlusion with minimal risk of ventricular fibrillation and neurologic sequelae.

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THE CREATION AND REPAIR OF INTERVENTRICULAR SEPTAL DEFECTS IN DOGS UTILIZING THE HEART-LUNG MACHINE

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SEVERAL different methods have been employed in attacking the problem of interventricular septal defects, but we feel a heart-lung machine which will oxygenate and pump adequate amounts of blood safely remains the ultimate goal. This group of experiments was undertaken to gain acquaintance with the problems inherent in application of our machine to this type of procedure and with an eye to clinical cases. Gibbon, Miller, Dobell, Engell, and Voight[1] reported a series of 20 dogs in which they used their heart-lung machine to close previously created interventricular septal defects, with eight deaths. Donald, Harshbarger, Hetzel, Patrick, Wood, and Kirklin[2] also closed interventricular septal defects using the Gibbon type heart-lung apparatus. Hypothermia was used by Taufic and Lewis[3] and by Scott, Collins, and Foster,[4] while Warden, Cohen, Read, and Lillehei[5] used controlled cross-circulation in the same type of work. Murray[6] described the use of a strip of fascia lata in the closure of interventricular septal defects without opening the ventricle in 1948.

METHOD

Mongrel dogs weighing from 9 to 33 Kg. are anesthetized with intravenous pentobarbital sodium and placed on controlled respiration. The right and left femoral veins and arteries are isolated in the groins and the right external jugular vein is isolated in the neck. The right chest is entered through the bed of the fifth rib and sling ligatures of umbilical tape are placed around the superior and inferior venae cavae adjacent to the right auricle. The azygos vein is tied. The animal is then given 2.5 mg. of heparin for each kilogram of body weight. A polyethylene catheter is inserted into the left femoral artery and attached to a Statham strain gauge so that blood pressures may be recorded throughout the procedure. Venous blood is collected from the animal by a plastic catheter (No. 14 Fr.), inserted into the superior vena cava through the external jugular vein, and by a second catheter into the inferior vena cava through the right femoral vein. A metal cannula is inserted into the right femoral artery to return the blood from the heart-lung machine to the dog.

A Foley catheter is placed within the right atrium, and the balloon distended to the point where it occludes the tricuspid orifice. During the ventriculotomy, blood returning to the right atrium through the coronary sinus is carried to the oxygenator through the lumen of the catheter.

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Supported by grants from the United States Public Health Service and the Life Insurance Medical Research Fund.

Presented in summary form at Surgical Forum of the Clinical Congress of American College of Surgeons, Chicago, November, 1955.

Received for publication March 5, 1956.

The dog's heart and lungs are excluded from the circulation by occlusion of the superior and inferior venae cavae with the sling ligatures. Venous blood flows by gravity through a constantly recording rotameter and is filmed on stainless steel screen discs which are slowly revolving in an atmosphere of oxygen at room temperature. The blood is collected below the discs and passes through a bubble trap, consisting of a stainless steel sponge coated with Dow-Corning Anti-Foam A. A modified Dale-Schuster pump forces blood back into the arterial system of the dog through the cannula in the right femoral artery. The flowmeter, oxygenator, bubble trap, and modified Dale-Schuster pumps have been described in detail in an earlier paper from this laboratory.[7] The assembled oxygenator is sterilized by autoclave, and the pumps and tubing are sterilized with 10 per cent formaldehyde solution. Eleven hundred milliliters of blood are required to prime the system. Clotting is prevented by the addition of 40 mg. of heparin (Connaught Laboratories) to each liter of freshly drawn arterial blood.

A 5 to 6 cm. incision is made over the outflow tract of the right ventricle. A defect, approximately 2 cm. long, is made in the interventricular septum so as to avoid the conduction system insofar as possible. The defect is closed with three to five interrupted silk sutures. The ventriculotomy is closed with interrupted silk sutures. The perfusion is terminated and the cannulae removed.

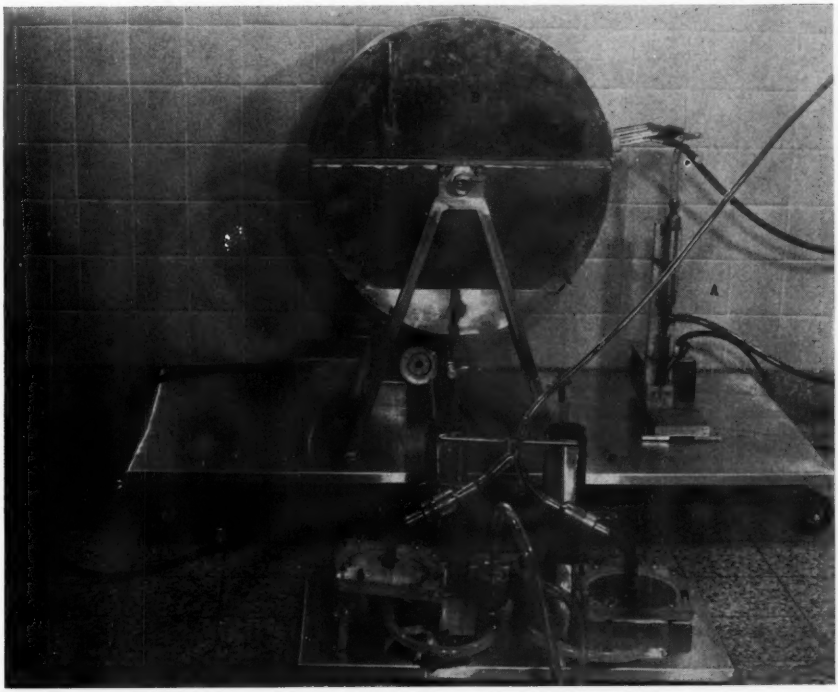

Fig. 1.—*A*, Flowmeter. *B*, Oxygenator. *C*, Bubble trap. *D*, Modified Dale-Schuster pump.

A protamine-heparin titration is performed on blood samples just before the perfusion ends to estimate the amount of protamine needed to return the clotting time to normal. The estimated protamine is given in 100 ml. of 5 per cent glucose in water over a period of approximately fifteen minutes. Subsequent protamine titrations are performed every twenty to thirty minutes for an hour, and additional protamine is given as needed. A fresh whole

TABLE I. PERFUSION DATA

DOG NUMBER	WEIGHT (KG.)	FLOW (C.C./MIN.)	ARTERIAL SAMPLES—PREPERFUSION					ARTERIAL SAMPLES—END OF PERFUSION						RESULT
			PH	HCO_3 (MEQ./L.)	PYRUVATE (MG %)	O_2 CONTENT (VOL. %)	CO_2 CONTENT (MM./L.)	PH	HCO_3 (MEQ./L.)	PYRUVATE (MG.%)	O_2 CONTENT (VOL. %)	O_2 SATURATION (%)	CO_2 CONTENT (MM./L.)	
36	14.6	—	—	—	—	—	—	—	—	—	—	—	—	Survival
131	19.5	800	7.23	26	0.7	—	24.62	7.36	16	1.0	13.98	81	14.55	Survival
132	25.7	750	7.07	31	—	—	27.93	7.59	14	—	20	108	11.50	Survival
144	15.5	400	7.53	—	—	—	—	7.46	8	—	20.39	92	7.2	Survival; bled
146	19.5	600	7.29	16	—	20.57	14.33	7.45	12	—	22.97	98	9.66	Died
150	21	550	7.48	20	—	19.13	15.53	7.55	13	—	21.2	99	9.09	Died
153	15.5	—	7.56	18	—	17.80	15.40	7.70	11	—	17.58	108	8.46	Survival
157	24	—	7.44	20	2.2	19.00	17.46	7.40	12	3.2	15.95	88	10.26	Survival
159	9	—	—	—	—	—	—	7.42	—	—	—	—	—	Survival
165	9.7	—	—	—	—	—	—	7.60	—	—	15.74	89	9.50	Survival
167	29.3	1500	7.37	14	—	21.44	12.52	7.58	7	—	18.88	95	6.90	Survival
168	33.5	800	7.34	16	1.9	23.33	14.12	7.37	—	2.2	11.09*	55	13	Survival
193	23.8	1000	7.58	20	1.2	19.95	16.73	7.59	16	1.9	16.2	90	12.90	Survival
194	28.2	800	7.43	21	1.2	20.90	17.80	7.53	16	2.2	18.6	85	12.40	Survival; bled
195	14	600	7.56	16	1.0	22.80	12.79	7.58	—	2.6	18.63	102	7.50	Survival
246	18.2	850	7.44	26	1.4	18.23	22.46	7.65	14	1.8	18.01	109	11.78	Survival
249	14.8	600	7.59	15	2.1	20.56	12.71	7.67	12	2.6	19.46	101	8.87	Survival
Average	19.7	770	7.42	19.9	1.47	20.34	17.26	7.53	12.6	2.1	17.91	96	10.24	15 Survived 2 Died

*Not included—technical error.

blood transfusion, amounting usually to one fourth to one third of the estimated blood volume, is given as soon as the protamine has been administered. A thoracostomy tube is inserted on either side and attached to water-seal drainage, and the chest is closed. During the postoperative period, a careful check is kept on the drainage from the chest and additional fresh whole blood is given as indicated.

The essentials of the heart-lung apparatus are demonstrated in Fig. 1,* and a diagram of the perfusion circuit is indicated in Fig. 2.*

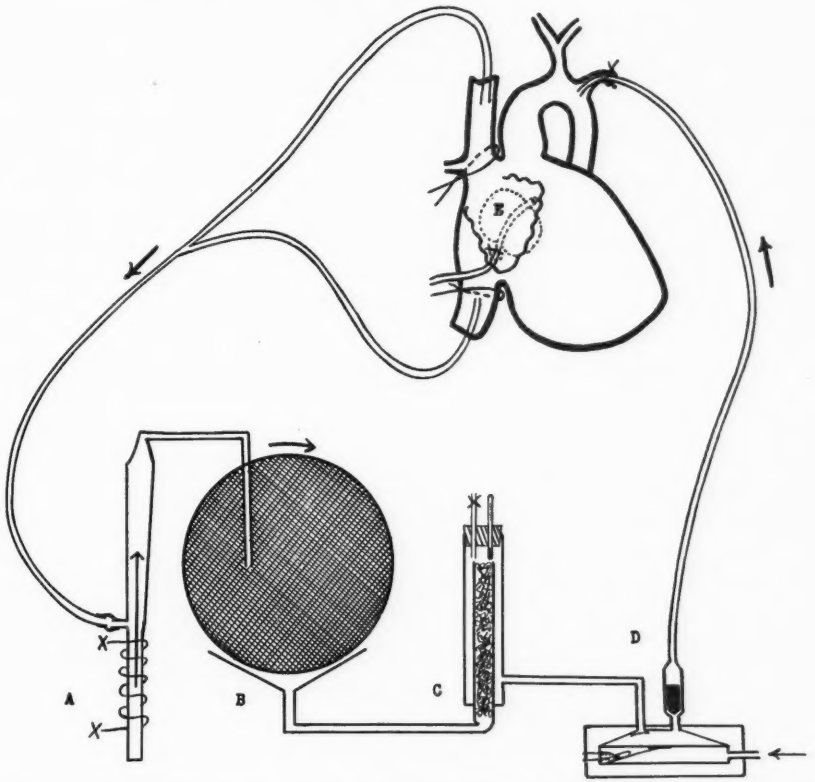

Fig. 2.—*A*, Flowmeter. *B*, Oxygenator. *C*, Bubble trap. *D*, Modified Dale-Schuster pump, compressed air enters at arrow. *E*, Foley catheter in right atrium.

RESULTS

Seventeen animals were operated upon as described. Fifteen survived and 2 died. One death resulted from a pneumothorax which developed when a thoracostomy tube became disconnected from the water-seal system in the early postoperative period. The second death resulted from occlusion of the chest drainage tubes, and the animal died of a hemothorax and bilateral compression atelectasis.

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Two animals required re-exploration for excessive bleeding from the chest. One dog lost 350 ml. of blood from the chest in a short period, and when re-explored was found to be bleeding from the tip of the auricular appendage. The second dog lost 500 ml. of blood from the chest in one hour, and upon re-exploration was found to be bleeding from a mediastinal vessel. Both dogs recovered after the second operation. In the remaining dogs the average postoperative blood loss into the water-seal bottles was 180 ml.

The average weight of the dogs was 19.7 Kg. The average flow rate during perfusion was 770 ml. per minute or 39 ml. per kilogram body weight per minute. The blood pressure averaged 80 mm. Hg systolic and 40 mm. Hg diastolic during the perfusion.

Arterial saturation during perfusion averaged 96 per cent for 16 of the dogs. The CO_2 concentration regularly fell almost 50 per cent below control levels. The blood pyruvate level rose from an average control level of 1.47 mg. per cent to 2.1 mg. per cent at the end of perfusion. The blood pH rose from the control average of 7.42 to 7.53 at the end of perfusion. The average total time of perfusion was thirty-eight minutes, and the average blood loss was 560 ml. during the cardiotomy. All the data are summarized in Table I.

DISCUSSION

The advantages in using a heart-lung machine in ventricular septal surgery, over other methods such as refrigeration and blind suture, are several. With it, intracardiac procedures can be carried out unhurriedly in a relatively dry field. Diagnosis of the type of lesion can be accurately determined and precise repair carried out only in the presence of direct vision. Perfusion during the procedure insures an adequate supply of oxygen to all tissues at all times.

There are hazards in the use of an extracorporeal system. The problem of uncontrolled bleeding following perfusion because of inability to restore the clotting mechanism to normal has been seen in the past but was not encountered in this group of animals. We feel that good metabolic preparation of the dogs, avoidance of excessively prolonged perfusion, operation of the apparatus so as to minimize undue trauma to the formed elements of the blood, accurate back-titration of heparin with protamine, and replacement of unknown clotting factors by fresh blood transfusion at the end of the procedure[8] are all factors in this accomplishment. Continued excessive postoperative blood loss from the chest tubes after the circulating heparin has been neutralized and fresh blood has been given is an indication for re-exploration of the subject.

Air embolism was not a problem in this group of animals. We feel that a system which uses gravity alone to drain the venae cavae is safer than pumping systems which reduce the pressure of contained blood below that of the atmosphere, for such low pressures invite bubble formation both from effervescence and from leaks into the system from the surrounding atmosphere. The mechanisms by which negative pressures are avoided have been previously described.[7]

Oxygenation at the end of perfusion averaged 96 per cent for 16 of the subjects. One dog. (No. 168) was not included in the average since the oxygenator was not functioning properly through a technical error. The level of fixed

acids rose during the procedure and tended to offset the average 50 per cent fall in CO_2 concentration. The blood pH rose from a control level of 7.42 to 7.53 at the end of the procedure. It does not appear to be necessary to add carbon dioxide to the oxygen run into the oxygenator. The mean control plasma hemoglobin was 18.8 mg. per cent, while the mean plasma hemoglobin at end of perfusion was 86 mg. per cent. This is far below the amount required to cause renal damage.[9]

Ventricular fibrillation occurred during cardiotomy in 6 of the 17 dogs, and was present thirteen to twenty-eight minutes. Undoubtedly, one factor in the initiation of fibrillation was injury to the conduction system at operation. No difficulty was encountered in defibrillating the hearts with electrical discharges of 0.1 second at 1.75 amperes. Undoubtedly adequate myocardial perfusion throughout was a factor in this ease of defibrillation, as Senning has shown.[10] Following defibrillation, the hearts developed a 3:1 atrioventricular block, initially. This shortly changed to a 2:1 block, and within a few minutes to a normal sinus rhythm.

The two deaths in this series emphasize the importance of postoperative care. The lungs must expand completely; all blood must be evacuated from the thoracic cavity; the tubes must remain patent; the position of the animal must be changed frequently.

The inflated Foley catheter in the right atrium serves to return the coronary blood flow directly to the oxygenator and materially reduces the over-all blood loss during the procedure. The coronary sinus return in a 15 Kg. dog during perfusion is from 40 to 50 ml. per minute (our measurements), and in large dogs is proportionately more. Blood from the suction bottle has on occasion been returned directly to the system and no difficulty has been encountered. This we prefer not to do as the average plasma hemoglobin of this blood is 325 mg. per cent, and we suspect such return to contribute to late problems of hemostasis. In general, the blood loss at operation becomes smaller as the techniques are mastered by the operators and operating time is reduced.

The average ventriculotomy incision in the dogs was 5.5 cm. in length. Speculation as to the ultimate fate of these wounds, and whether or not aneurysms would develop, is still unsettled, although they have not been seen in dogs sacrificed up to twelve months after ventriculotomy.

CONCLUSION

The heart-lung apparatus previously described by this group has been employed in the creation and repair of interventricular septal defects in 17 consecutive dogs, with two deaths. There were no deaths as a result of machine failure.

Advantages of a heart-lung machine as outlined have been that it is possible to operate within the heart in an unhurried and safe manner in a relatively dry field, and that diagnosis and repair of the lesion can be carried out more precisely than by blind or hasty methods.

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Announcements

THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

Notice of Annual Meeting

The Thirty-seventh Annual Meeting of The American Association for Thoracic Surgery will be held May 4, 6, and 7, 1957, in Chicago, Illinois. Headquarters will be at the Palmer House.

Requests for Hotel Reservations

These should be mailed directly to Mr. Edward Langford, Reservations Manager, Palmer House, Chicago. Please mention this Association, the type of accommodation desired, the date, and approximate hour of arrival and departure. If accommodations are desired elsewhere in Chicago, please communicate directly with the hotel of your choice.

Thoracic Surgery Forum

The Thoracic Surgery Forum will be continued as a special session at the 1957 meeting. The Forum is primarily for the presentation of short papers on current thoracic research, experimental problems, anatomical studies, and modified or new surgical techniques. The inclusion of any considerable amount of clinical material in these reports makes the choice more difficult and the Program Committee reserves the right to reject such papers, or to suggest their transferal to the Regular Program.

Papers at this session will be limited to ten minutes, including the showing of lantern slides or other illustrative material. At the discretion of the President, three minutes may be allowed as the maximum discussion for each paper.

All Thoracic Surgery Forum papers will be published together in one issue of the JOURNAL. Maximum length: 3000 words without illustrations. If illustrated, an appropriate number of words must be subtracted for each cut used.

Abstracts of Papers

Abstracts of all papers for presentation at the 1957 meeting must be received on or before Dec. 15, 1956, otherwise they will not be considered by the Program Committee.

Abstracts should be labeled "For Thoracic Surgery Forum," or "For Regular Program." The abstracts should contain from 200 to 250 words and accurately reflect the contents of the completed paper.

Five, repeat, five copies of *each* abstract must be sent to Miss Ada Hanvey, Administrative Assistant, The American Association for Thoracic Surgery, 600 South Kingshighway, St. Louis 10, Missouri.

Those on the program are reminded that papers presented at the meeting *must* be handed to the secretary immediately after their presentation. If they are not ready at that time there is a chance that they will not be published in THE JOURNAL OF THORACIC SURGERY.

Motion Picture Session

Provisions have been made to show a limited number of motion pictures to be selected on a competitive basis. *The films themselves,* together with descriptive material concerning length of presentation, etc., must be received by Dr. Karl P. Klassen, The Ohio State University, Columbus 10, Ohio, before Dec. 15, 1956.

It is planned to run the motion pictures in a smaller room at the same time as the scientific sessions. If the films are well labeled, it will not be necessary for the author to be present for comment.

Applications for Membership

Applications for Associate Membership in the Association must be received by the Membership Committee not later than Dec. 15, 1956, otherwise the application will be deferred for consideration until the 1958 meeting.

Applicants must be sponsored by three Active or Senior Members of the Association. In addition to the signatures on the application form, the sponsors will forward a *separate* letter concerning the applicant directly to:

Dr. O. T. Clagett
Chairman of the Membership Committee
Mayo Clinic
Rochester, Minn.

Sponsors are reminded that *new* letters of recommendation must be forwarded to the Membership Committee should their applicants be held over for reconsideration a second year. The new letters of recommendation should also be sent to Dr. Clagett, the Chairman of the Membership Committee.